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PELLAGRA FOLLOWING OPERATION FOR GASTRIC ULCER; THE SIGNIFICANCE OF ANALYSIS OF GASTRIC CONTENT IN THE DIAGNOSIS OF CARCINOMA OF THE STOMACH

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PELLAGRA FOLLOWING OPERATION FOR GASTRIC ULCER

Case 1.—A woman, aged forty-six years, first came under observation at the clinic June 17, 1929. In February she had noted melena after dietary indiscretions and the use of purgatives. Since then, she never had felt quite normal. May 18, she had had a second, more severe attack of melena, which had lasted from three to four days, following which she had been considerably prostrated. The attending physician had administered a liter of blood by transfusion. She had been obviously anemic since the last hemorrhage.

The examination, with the exception of the anemia, gave negative results. The concentration of hemoglobin was estimated at 50 per cent, erythrocytes numbered 4,110,000, and the leukocytes 11,900, in each cubic millimeter of blood; the color index was 1.6+. Analysis of gastric content disclosed total acidity of 60 and free hydrochloric acid of 24 in terms of cubic centimeters of tenth-normal sodium hydroxide. No blood or remnants of food were noted in the gastric content and the filtrate measured 60 c.c. Roentgenoscopic and roentgenographic examination revealed signs of an ulcerating lesion high in the

cardiac end of the stomach. The increased size of the crater was suggestive of a malignant condition.

At operation, performed June 22, a freely movable, ulcerated lesion in the fundus, surrounded by a mass about 7 cm. in diameter, was seen. Jejunostomy after the method of Witzel was performed.

Postoperative treatment included jejunal feedings consisting, daily, of cooked cereals, 2 ounces (60 c.c.) of orange juice, and eggnog, malted milk, cream soup, milk and cream, and canned fruit juices, a total of 1,600 calories. Owing to the nausea induced by the mixtures of egg and milk, the patient restricted her food to about half of the prescribed total daily intake.

Diarrhea, which lasted only for five days, appeared a month prior to the patient's second appearance at the clinic, September 10. This condition was attributed to the excessive amount of cream introduced into the tube. Acute proctitis, also acute stomatitis and glossitis, roughening and fissuring of the knuckles of both hands, with sharp delineation of these lesions at the wrists, appeared two weeks later.

The impression, which was concurred in by the dermatologists, was that a pellagrous type of avitaminosis existed. The concentration of hemoglobin was estimated at 67 per cent; erythrocytes numbered 4,710,000, and leukocytes 6,100 in each cubic millimeter of blood. Following jejunal feeding, analysis of gastric content disclosed total acidity of 24, and absence of free hydrochloric acid. As determined by fractional analysis after a test meal, the content of free hydrochloric acid ranged from 0 to 12 per cent. The patient was given a diet high in vitamin G, which included scraped beef, fresh fruit juices, and Harris' brewers' yeast; the daily food values were equivalent to 2,400 calories. The patient's weight was maintained on this treatment. She improved markedly and the acute condition in the mucous membranes subsided in less than a week. The improvement of the lesions on the hands was more gradual. A roentgenoscopic examination, made September 23, showed that the lesion in the stomach still persisted and was of about the original size.

By request, the patient returned the third time, November 12, 1929. Although she appeared somewhat anemic, she had gained 15 pounds during the previous six weeks and was in excellent spirits. She had no digestive disturbances and she had more appetite. She was taking food both by mouth and by the jejunal tube. The tube caused considerable local discomfort, and it was removed. The patient's coöperation was satisfactory. Orange juice, milk, cream, meat balls of fresh beef, meat juice, tomato juice, and brewers' yeast made up a major portion of her diet. Hemoglobin was estimated at 52 per cent; erythrocytes numbered 3,540,000, and leukocytes 7,800 in each cubic millimeter of blood. Although the blood count was not as favorable as at the last visit, roentgenoscopic examination showed that the lesion was greatly reduced, the stomach was flexible and the crater of the ulcer was shallow. The patient was dismissed from hospital, with instructions to follow the same diet high in vitamins. In addition, ferric citrate and alkalies were prescribed.

At reëxamination, February 3, 1930, it was observed that the patient had gained in weight from a minimum of 117 pounds in September, 1929, to 149.5 pounds. Her weight prior to operation was 139 pounds, and her usual weight averaged 152 pounds. Her color was good; concentration of hemoglobin was estimated at 12.6 gm.; erythrocytes numbered 4,500,000 and leukocytes 10,000; the percentage of neutrophils was 70.5 and of lymphocytes 21.5. Fractional analysis of gastric content revealed total acidity of from 20 to 46 and free hydrochloric acid of from 10 to 28. The patient had no subjective complaints. Examination of the feces for occult blood gave a negative result. Roentgenoscopic examination of the stomach showed that the lesion was still present, but that it was again somewhat reduced since the previous examination. It was decided to give the patient a diet that was more specific for ulcers of this type for a period of at least three weeks in the hope that the niche would disappear entirely, as the accumulating evidence favored a benign rather than a carcinomatous lesion.

Students of nutrition and of nutritional diseases are aware that these diseases may arise from many causes. They may be

the result of certain therapeutic diets, such as those for ulcer, those for functional gastro-intestinal conditions, or the ketogenic diet for epilepsy; they may arise from voluntary dietary restriction over a considerable period of time, or they may be a serious complication of malignant and benign obstructive lesions in the upper part of the digestive tract. Under such circumstances, scurvy, pellagra, and so forth, may be looked on as diseases with universal distribution. In the enthusiasm for controlling an obvious functional condition, or for causing a lesion to heal, one sometimes ignores the sustenance of the patient. Such indifference is probably natural, by virtue of the fact that an actual deficiency disease of a readily recognized type may occur only after a long period of deprivation in most instances, and active therapeutic measures usually are only temporary. Recent writers have emphasized the fact that the ultimate effect of any diet that is deficient in accessory food factors, regardless of how successful it is in combating manifestations of the disease under treatment, must be carefully considered. It is also reasonable to presume that the ensuing effects might be detrimental to the cure or to the relief of the lesion or condition under treatment.

Jejunostomy for extensive benign ulcerating lesions situated high in the stomach is effective. The lesion has been known completely to disappear within three weeks after the operation, frequently never to return.

In this case the state of avitaminosis was so acute, and the lesions caused so much discomfort, that at the outset, more exacting clinical studies to determine if possible the actual nature of the gastric lesion, were not feasible. It is reasonable to presume that failure of the ulcer to heal, if it was benign, was due to the markedly disturbed nutrition. In all ill-defined complaints, usually called neurasthenia, and in which symptoms may be referable to the digestive tract, or to the organs of special sense, or in which there is obscure anemia, nervousness, disturbance of the endocrine functions, lowered resistance to infection, or disturbances in growth and sexual function, the possibility of an inadequate diet should be considered as a cause. Those instances of pellagra sine pellagra are of interest. The average American

diet is low in residue, in vitamins, and in alkaline ash-forming foods, and in certain sections of our country, or under certain unfavorable economic conditions, avitaminosis fundamentally plays a large part in the complaints presented by patients. Diets following gastrostomy or jejunostomy have been well standardized, both as regards adequate intake of calories and content of vitamins, so that the weight and health of the patient may be maintained over a long period, even if it is necessary to continue the diet. Failure on the part of the patient to coöperate, or inability, for one reason or another, to utilize the food, may give rise to serious complications if they are left to progress unrecognized.

This patient may have had a predisposition to dietary deficiency disease. Perhaps also, if the opinions of some authorities are correct, she had predisposition to gastric ulcer. Since girlhood, carbohydrates had made up a large portion of her diet. Her sprees of eating confectionery precipitated the gastric hemorrhages. Milk and some fresh fruits were agreeable to her, but were taken daily in inadequate amounts. Fresh meat, butter, eggs, and vegetables were always eaten sparingly.

THE SIGNIFICANCE OF ANALYSIS OF GASTRIC CONTENT IN THE DIAGNOSIS OF CARCINOMA OF THE STOMACH

Case 2.—A man, aged sixty-five years, entered the clinic November 11, 1929, with the complaint of digestive disturbances for many years, which had been more marked during the four months prior to examination. The symptoms complained of consisted of flatulent epigastric distress, described as "pressure and fulness." There was some distention of the upper part of the abdomen, which appeared soon after meals, lasted for several hours, and as a rule was associated with moderate pyrosis. Fried food had aggravated this tendency, for the relief of which tablets containing soda, magnesia, and bismuth had been taken. There had been no nausea, vomiting, acute pain, or localized tenderness, and no evidence of bleeding from the gastro-intestinal tract. The patient's appetite was impaired little, if at all, and there was no particular distaste for meat or other food. He had been markedly

constipated for a long time. In the diet, meat and potatoes had been favored, to the exclusion of fruit, vegetables, milk, and eggs. He had been under business and emotional strain for years. Thirty years before examination he had had a nervous breakdown and had rested for a year, during which time he had felt generally run-down and nervous, had had much gastric distress, and had lost 40 pounds in weight. However, he had recovered and regained the weight he had lost. In December, 1928, as the result of many business trips throughout the country, during which time he had been subjected to vagaries in diet, the patient had an attack of nausea and vomiting, and icterus to a moderate degree which had lasted for a fortnight. He had noted that the stools were light and that the urine was dark. There had been moderate transient elevation of temperature, but absence of chills, localized pain, tenderness, and colic. The patient had recovered from this indisposition promptly and had felt better than usual until the onset of the disturbances four months prior to his coming to the clinic. The patient had been obese for years, but thought that he might have lost from 5 to 10 pounds in the five months prior to admission. His strength and general appearance were as usual. Five weeks before admission, during a rather strenuous fishing trip, he had had an exacerbation of the symptoms before mentioned. Just prior to coming to the clinic he had consulted a physician, who had referred him to a roentgenologist. The latter had reported considerable barium retention in an otherwise normal stomach and duodenum, but a cholecystographic examination had appeared to show shadows in the region of the gallbladder, which had been interpreted as gallstones. The patient's personal habits were better than the average, and there was no history of carcinoma, tuberculosis, diabetes, or psychosis in his antecedents or in his immediate relatives.

The patient was an obese man, weighing 202.5 pounds. With the exception of mild tenderness and a sense of resistance in the right epigastric region, and epidermophytosis of the feet, nothing unusual was found. An estimation of the hemoglobin, by the photo-electric method of Sanford and Sheard, revealed 13.6

gm. for each 100 c.c. (about 82 per cent); erythrocytes numbered 4,060,000, and the leukocytes 5,500 in each cubic millimeter of blood. The concentration of blood urea was 30 mg. for each 100 c.c. The carbon dioxide combining power of the blood plasma was 64.3 volumes per cent. Urinalysis, blood pressure, the Wassermann reaction of the blood, cardiovascular studies, and tests of reflexes and sensations gave results within normal range. Analysis of gastric content was made, November 14, one hour after the usual test meal of arrowroot wafers and water had been given, and fourteen hours after a so-called "motor" meal, that is, a meal given in the evening, the residue of which is aspirated from the stomach the next morning to determine whether or not there is undue stasis of gastric content. The analysis disclosed total acidity of 90, in terms of cubic centimeters of tenth-normal sodium hydroxide, absence of free hydrochloric acid, some bile, fine remnants of food of the motor meal, lactic acid, and Oppler-Boas bacilli. The total quantity aspirated was 375 c.c. November 22, a second analysis of gastric content gave the following results: The quantity removed was 325 c.c.; the total acidity was 76, free hydrochloric acid was absent, there were a few remnants of food, some altered blood, a positive benzidine reaction for blood in the filtrate, some mucus, lactic acid, Oppler-Boas bacilli and yeast cells. November 28, fractional analysis after a test meal disclosed total acidity ranging from 24 to 28, absence of free hydrochloric acid in five specimens secured by aspiration and a total quantity measuring 163 c.c. The chemical and microscopic observations were similar to those of the previous tests. November 11, the roentgenoscopic examination showed that the stomach and duodenum were normal, except for the presence of some residue of barium. A week later the results of a roentgenoscopic and roentgenographic study were reported as negative. On cholecystographic study, the gallbladder was shown to be functioning poorly, but no evidence of stones was reported. November 22, a final critical roentgenoscopic examination of the antrum was made for neoplasm; this did not result in tangible evidence of a lesion. Notwithstanding this, a provisional diagnosis was made of carcinoma of the stomach with marked im-

pairment of gastric motility, and probable chronic disease of the gallbladder, and a surgeon's opinion was requested. During the period of observation (two weeks) the patient made definite clinical improvement and gained about 5 pounds in weight. This could have been attributed to rest, frequent lavage, and the somewhat more suitable and varied diet given while the patient was under observation. Because the repeated roentgenologic observations were favorable, and because of the recent improvement and the approach of the Christmas holidays, the patient wished to postpone surgical exploration, which had been recommended largely in view of the observations noted on analysis of gastric content. He was advised to return by the last week of December, at the latest.

The patient returned to the clinic December 30. During the interval of five weeks he had lost weight and strength; anorexia, nausea, and a distaste for meat had been present for a month. Vomiting, preceded and associated with nausea, had been present twice. On the last occasion the vomitus had been of a retention type, but in neither instance had it been grumous and the bowel movements never had been tarry. The constipation had been aggravated. In view of the patient's idiosyncrasies, the soft diet recommended for him had not been relished.

Examination disclosed definite evidence of disturbed nutrition; the patient now weighed 189 pounds, and was pale. The hemoglobin was 12.9 gm.; erythrocytes numbered 4,710,000, and leukocytes 8,100. Examination of the organs of the thorax and abdomen, and the lymph nodes and rectal shelf gave negative results. Analysis of gastric content, December 31, showed a total acidity of 72, no free hydrochloric acid, and the total quantity removed was 2,240 c.c. The gastric content was rancid and contained fine remnants of food. The filtrates gave a strong benzidine reaction for blood. Lactic acid also was present. Following a cleansing lavage, roentgenoscopic examination showed that the stomach was slightly enlarged, but no defect in the outline of the lumen of either the stomach or the duodenum was present; peristalsis was normal throughout the viscus, and following a barium meal, the emptying capacity of the stomach

seemed unimpaired. A roentgenologic diagnosis of a normal stomach was made.

On the basis of the previous clinical diagnosis, an exploratory operation was performed, January 3, 1930. A carcinoma, 2.5 cm. in diameter, situated on the greater curvature near the pylorus, was found. The muscularis was extensively involved, but no lymphatic involvement was noted. There was no evidence of distant metastasis. The gallbladder appeared normal, and no stones could be palpated. Posterior partial gastrectomy by the method of Polya was performed, in which almost three-fourths of the stomach was removed. The patient recovered and convalescence was uneventful.

The general examination did not disclose tangible evidence of a carcinoma of the stomach. The symptoms could have been caused as well by cholecystic disease as by a new growth. The fact that the patient complained of flatulence for years made the more recent complaint of four months' duration of less significance. The retention type of vomitus on one occasion, and the progressive decline in health, as evidenced on the patient's last admission to hospital, caused carcinoma to be suspected. From the outset, the results of the analysis of gastric content were significant. High total acidity, in the absence of free hydrochloric acid, and evidence of retention, invariably is significant of carcinoma, with actual pyloric obstruction or marked impairment of gastric motility. The previous diagnosis of disease of the gallbladder also was considered, and was confusing, but there was no evidence of such disease at the time of the operation. Although cholecystic disease may be associated with achlorhydria in from 13 to 18 per cent of patients with disease of the gallbladder, it rarely engenders pyloric obstruction or marked impairment of gastric motor function. In every case of gastric anacidity it is essential to distinguish a malignant from a benign form of achlorhydria or achylia. In this case evidence seemed overwhelmingly in favor of a malignant form of achlorhydria.

Occasionally, chronic gastritis associated with mucosal erosion may be associated with the presence of blood and anacidity, but all obstructing lesions associated with anacidity

invariably are carcinomatous. This is of significance to the clinician, because often the roentgenologist will report an obstructing lesion at the pylorus in the presence of achlorhydria and ascribe it to duodenal ulcer. Such instances are frequently seen in elderly patients with a short history of gastric disorder, and analysis of gastric content reveals retention, anacidity, and often other chemical and microscopic features characteristic of carcinoma. With the rarest exception, such lesions involve the pylorus rather than the duodenum and are carcinomatous rather than syphilitic or tuberculous. Detection of neoplasms in the upper third of the stomach by means of roentgenograms is admittedly more difficult than detection of lesions in the lower or middle third of the organ by the same means. This is because of the greater difficulty of filling completely the upper third of the stomach with the opaque meal. Of especial value in this connection is the article which Carman presented in 1923 before the American Gastro-Enterological Association, entitled "Technical Aids in the Roentgen Demonstration of Lesions High in the Stomach and on the Posterior Wall." As a rule, fluoroscopy will fail much more frequently in lesions which are high or on the posterior wall than in lesions at or near the pylorus. In such cases the anacidity and the presence of blood in the gastric content are on occasion the most tangible clues as to the presence of carcinoma. As gastric motility is never impaired in such cases, the observations relative to the stomach are practically limited to the features of achlorhydria and blood. With this evidence, repeated examinations and special maneuvers by the fluoroscopist occasionally will enable him to visualize the lesion, which may have been missed on the initial examination. Intra-abdominal lesions difficult to visualize by means of the roentgenogram, and which have the clinical earmarks of carcinoma, invariably are inoperable. Even if the growth is removed it usually is of such extent or in such a situation that recurrence takes place early. In the days before the advent of roentgenoscopic examination of the stomach as a routine measure, and especially before it became such a highly developed and accurate procedure in expert hands, the clinician had less doubt about the condition present

when the analysis of gastric content gave results such as those in the case presented. The very fact that roentgenoscopy of the stomach, in the detection of malignant lesions, has reached such a high degree of efficiency, occasionally may give rise to doubt when the lesion is not visualized. On the contrary, it is a means of rapid and accurate diagnosis in most instances. In some cases, gastroscopic examination has been carried out in order to make the diagnosis clear in lesions difficult or impossible of visualization by means of roentgenograms.

Of added interest in the case was the constant evidence of motor impairment of the stomach on analysis of gastric content, and the inconstant evidence of it on roentgenographic examination. There was no retention, at six hours, of the barium meal that was deliberately administered on one occasion following a negative roentgenographic study. In fact, the results of studies of motor function are usually the reverse, especially in dealing with primary lesions of the stomach and duodenum of all types. It is less true in patients with late postoperative gastric dysfunction or recurrent lesions. This discrepancy in the group first mentioned is more apparent than real, because the ordinary motor meal is withdrawn after a much longer interval, usually twelve to fourteen hours, whereas the evidence of retention of barium is sought for six hours after administration of this meal. Another feature of clinical interest is the fact that marked motor impairment may be present in the absence of mechanical motor obstruction at the pylorus, as in this case. Almost half of the cases at the clinic in which there has been evidence of abnormal retention of barium or food in the stomach have occurred in carcinomatous as well as benign lesions not actually involving the pyloric outlet, or remote from it.

This case emphasizes the fact that diagnosis depends, not on any one factor, but on all available factors. When the roentgenograms are not in accord with the clinical evidence, the roentgenologist should be given the opportunity to reëxamine the patient as often as he thinks necessary. If, then, the roentgenologic evidence is not satisfactory it should be given secondary consideration in the diagnosis.

PEPTIC ULCER AT THE JUNCTURE OF THE ESOPHAGUS AND CARDIA; ULCERATION AT THE ESOPHAGUS

GEORGE B. EUSTERMAN, HERMAN J. MOERSCH, AND JOHN D. CAMP

PEPTIC ULCER AT THE JUNCTURE OF THE ESOPHAGUS AND CARDIA

Case 1.—A woman, aged twenty-eight years, first consulted us in April, 1924. She had had dysphagia for twelve years. Investigation disclosed the presence of a cardiospasm with moderate dilatation of the esophagus. With the Plummer dilator the cardia was dilated to 28 feet water pressure without incident, and the dysphagia was relieved. Further dilatations were made in September, 1924. In September, 1925, examination revealed normal conditions.

The patient reported again in November, 1929. Three months prior to this, she had awakened early one morning with a diffuse epigastric gnawing sensation which lasted until noon. Discomfort was relieved temporarily by eating. The patient had a second similar, less marked experience several weeks afterward. Since Thanksgiving, 1929, she had had three attacks of hematemesis without preceding or associated epigastric pain. These attacks were followed by tarry stools, and on one occasion she fainted. The hemorrhages would "clog up the esophagus so that swallowing was difficult." This loss of blood was followed by anemia that was obvious. The patient had had epistaxis all her life, which had become less marked in recent years. A history of familial epistaxis, hemophilia, purpura, or other dyscrasia could not be disclosed, and there was no apparent telangiectasis.

Examination revealed an anemic young woman with an asthenic habitus. The heart, lungs, abdomen, organs of the pelvis, reflexes, and sensations objectively were negative. The hemoglobin was 55 per cent; erythrocytes numbered 3,870,000,

and leukocytes 9,800. There were enlarged venules of the left side of the cartilaginous septum anteriorly, which the rhinologist thought probably were the source of the nasal hemorrhages.

December 2, a number 41 French sound, passed into the stomach, met with little obstruction at the cardia, but some bleeding was noted. Examination, December 12, did not show evidence of a lesion in the esophagus, but blood could be seen coming irom the stomach. The stomach was reëxamined with special reference to the cardia, as a previous roentgenologic examination gave no definite evidence of a lesion. This examination revealed the niche of a small ulcer on the lesser curvature of the stomach, apparently at the juncture of the esophagus and cardia proper. There was also slight lagging of the barium meal at the cardiac juncture.

At the end of three weeks' medical treatment in hospital, during which time the patient received foods containing adequate vitamins and iron, the niche completely disappeared, with corresponding clinical improvement. Blood persisted in traces in the feces during the first week of treatment, but was absent thereafter. Aspiration of gastric contents to determine the effect of treatment revealed adequate free hydrochloric acid at the outset. The patient was dismissed from hospital, with instructions to continue the diet, and to continue taking alkalies in moderate doses, for a year, as is the rule.

The case is of interest chiefly because the lesion under consideration was situated higher in the pars cardiaca than any previously visualized or demonstrated at operation. It is well known that the site of the majority of gastric ulcers is in the middle third of the stomach in the vicinity of the incisura angularis. The relation of this lesion to the pre existing cardiospasm is doubtful, in spite of its high situation, as the association of cardiospasm of such duration and degree with the ulcer is conspicuous by its absence. It is also extremely doubtful that trauma from instrumentation incident to the treatment for cardiospasm played a part in the cause, because of the interval that had elapsed since the last dilatation, because of the early stage of the lesion, and finally because treatment for a large

series of cases of cardiospasm has never been known to cause a peptic lesion of this nature in this situation, or in the esophagus proper. The unusually high site of the lesion in the cardia and its close proximity to the esophagus was exemplified by the fact that during each period of hematemesis the blood clots would apparently so clog the esophagus that the patient temporarily could not swallow food, and moreover under fluoroscopic examination the niche appeared above the level of the diaphragm during inspiration and at its level during moderate expiration. The response to medical treatment was prompt and satisfactory, and it is felt that permanent cure of the ulcer without surgical interference will be accomplished if the coöperation of the patient is satisfactory.

This case and the one following make a fitting introduction to a brief discussion of esophageal peptic ulcer, concerning which there is still much disagreement among authorities.

ULCERATION OF THE ESOPHAGUS

Case 2.—A physician, aged sixty-nine years, first consulted us August 14, 1929, with the complaint of disturbance in the upper part of the epigastrium, of two years' duration, and dysphagia. There was a history of diabetes in three generations on the paternal side. The patient's mother died of cerebral hemorrhage at the age of sixty-eight years. The patient had had diphtheria in childhood, typhoid fever when aged sixteen years, and three attacks of pneumonia and influenza since 1918. The patient was active both professionally and socially, had epicurean tendencies, was in constant attendance at banquets, and partook freely of food, tobacco, and alcohol on such occasions. About two years prior to admission, while riding horseback, the patient felt that he had strained his back, as he experienced pain in the lower thoracic region of the spine which eventually radiated upward and forward, localizing in the upper part of the epigastrium in which it had persisted. The pain was usually of a dull, heavy nature associated with local tenderness, and radiated along both costal arches. It was more marked two or three hours after meals, and was relieved by soda, bromoseltzer and aspirin, but

was not relieved by food. This pain would disappear for two or three weeks, then reappear to remain for a week. Several months after the onset of this pain, the patient experienced dysphagia at intervals, especially if he ate meat heartily or if he partook of a hard roll. At times he would have "painful spasms" in the upper part of the epigastrium, associated with dysphagia, and would vomit all the food eaten. These spasms were not always associated with the pain, which appeared about two or more hours after eating. After a hearty meal in the evening, the patient might be awakened at 12 m. or 4 a.m., especially if lying on the left side, by marked discomfort in the epigastrium and along the borders of the ribs on both sides. During the eighteen months prior to admission he had lost 15 pounds in weight.

Examination showed moderate peripheral sclerosis, much dental repair, slight epigastric tenderness, and moderate prostatic hypertrophy. The color was good. The heart and lungs were objectively normal, but a roentgenogram of the thorax showed moderate calcification of the arch of the aorta. There was no substernal pain with posterior radiation. Roentgenograms of the esophagus showed a filling defect in its lower third which was thought to be of a carcinomatous nature. Dilatation revealed a short stricture in the lower part of the esophagus about 14 cm. from the incisor teeth. This was dilated with ease to 45 French without bleeding, and a 33 French sound was passed through the stricture without meeting obstruction. Two days later esophagoscopy revealed extensive annular ulceration of the lower part of the esophagus with partial reduction of the lumen of the tube. The lesion was considered benign. Two weeks later a second examination showed that all the ulceration had disappeared at the site of the stricture and it was felt that the previous ulceration was the result of instrumentation. In the interval the patient had been placed on a bland diet, low in residue.

The patient returned for examination December 3. He had improved considerably and the dysphagia had disappeared, but after a hearty meal, which included alcohol and tobacco, he would awaken from 12 m. to 4 a.m. with discomfort if lying on the left

side. Alkalies in large amounts, or codeine, would give complete or partial relief. Partaking of meats tended to provoke epigastric distress two to three hours after eating. Roentgenograms of the esophagus and stomach revealed no abnormalities. A 45 French sound was passed with very little obstruction and no bleeding.

It is obvious that the two cases reported differ in their clinical aspects. In the latter case the absence of a demonstrable ulcer in the stomach or duodenum, and the presence of annular ulceration and a short stricture in the terminal portion of the esophagus, with the history presented, justify the presumption at least that an ulcer of the esophagus was or had been present.

Experience has shown that, in the large group of patients suspected of having gastric or duodenal ulcer, dysphagia or odynophagia rarely develops at any stage, so that the frequency of esophageal peptic ulcer is debatable on clinical grounds. It is our opinion that such cases are relatively rare. Our experience has been confined to single or multiple, large or small, superficial erosions which are often incident to cardiospasm or which may be the result of trauma. The morphology of these ulcers has no resemblance to chronic peptic ulcer, and they are not discernible roentgenologically. There is one exception to this generalization, and it may be regarded as a clinical curiosity, for there is on record one case of an ulcer which had perforated the esophageal wall and formed an accessory pocket.

The following case history is perhaps even more illustrative of the subject, although it has not been definitely decided that the condition should be classified as an esophageal ulcer. The patient had dyspepsia of the chronic flatulent, hyperacid type, dysphagia, hematemesis, a lesion which was nonulcerating, but bled easily, and which apparently infiltrated the walls of the lower part of the esophagus. Roentgenograms disclosed the presence of the lesion with eventual stricturing, which responded favorably to treatment.

Case 3.—A man, aged fifty-six years, first came under observation in November, 1922. He had always been a hearty eater, and since early manhood had been subject to pyrosis and

to gaseous distress localized in the epigastrium. These disturbances appeared soon after meals and were relieved by taking more bland food or soda. For a period of two weeks prior to admission the symptoms had increased in severity. Recently the patient had had some dysphagia, also a feeling of epigastric fulness on a third of the amount of food formerly taken, and a retrosternal feeling of weight if he remained seated or inactive after meals. Six months previously, without apparent cause, he had vomited continuously for two days, during which time he could not even retain water.

Examination did not disclose abnormalities. Moderate gastric hyperacidity with considerable hypersecretion (350 c.c.) was noted but roentgenoscopic examination of the gastroduodenal area gave a negative result. An esophagoscopic examination was requested but the patient demurred.

On a bland diet low in calories and the use of alkalies, bismuth powder and atropine sulphate, the patient made considerable symptomatic improvement. He again reported for examination in March, 1929, because of aggravation of the dysphagia, pyrosis, flatulence, substernal pain, sometimes spasmodic in character, and substernal pressure of a progressive nature. Hematemesis in repeated small amounts had also occurred, with resulting anemia.

Gastric analysis showed marked hyperacidity, and roentgenograms disclosed that the duodenal cap appeared to be deformed. Esophagoscopy, performed April 17, revealed a firm, nonulcerated, but easily bleeding lesion, which infiltrated the walls of the lower part of the esophagus and which reduced the lumen of the tube to a fourth of its usual diameter. Tissue removed for diagnosis proved to be of an inflammatory nature. Fluoroscopic and roentgenographic examination showed a constant slight irregularity and spasm of the terminal portion of the esophagus which strongly suggested the presence of a nonmalignant lesion. The short stricture situated just above the cardia was dilated with ease to a 45 French sound. Two months later roentgenographic examination disclosed only slight narrowing of the lower third of the esophagus, with no deformity persisting in

the duodenal cap. January 17, 1930, an esophagoscopic examination revealed the persistence of some stricturing at the original site, and on approaching the involved area some bleeding but no evidence of deep ulceration was noted. Roentgenographic examination of this area, and the stomach and the duodenum, three days later gave essentially negative results.

CARCINOMA OF THE PROSTATE GLAND WITH EARLY AND EXTENSIVE METASTASIS TO THE CERVICAL, AXILLARY, AND INGUINAL LYMPH NODES

GEORGE B. EUSTERMAN AND S. FRANKLIN ADAMS

A farmer, aged forty-seven years, came to the clinic complaining of pain in the upper left quadrant of the abdomen. The health of the patient had previously been good with the exception of a mild attack of influenza. Two months before his appearance at the clinic, after a day of heavy physical work, he was seized with a severe pain in the upper left quadrant of the abdomen, which radiated around the costal margin to the back. Slight relief was obtained by flexing the knees on the abdomen. The pain persisted until the following morning, when a physician was called and morphine was given. After a few days, he felt better and was able to do light work, but was careful to avoid any exertion, as otherwise the pain would return. Five weeks before coming to the clinic he was forced to give up all work and two days before another agonizing attack of pain occurred, to alleviate which morphine was again required. Since the beginning of the illness, the patient complained of difficulty in passing urine. Blood or stones were not passed. The patient had lost 25 pounds in weight during the last two months.

Examination disclosed a number of discrete, hard lymph nodes in the left cervical region. There were similar nodes in the left axilla, and in the left and right groins. The prostate gland was moderately enlarged, somewhat nodular, and very hard; the growth had broken through the capsule. There was some infiltration of the vesicles. A specimen of urine contained considerable blood. The blood count and differential smears were normal. The Wassermann reaction of the blood was negative. A roentgenogram showed metastasis in the first and second

lumbar vertebrae. A lymph node was removed from the left supraclavicular region; microscopic examination showed adenocarcinoma, graded 3.

This case illustrates a point made by Young, that lymphatic or bony metastasis may give the first symptom of carcinoma of the prostate gland. Ewing stated that carcinoma of the prostate gland is less likely to involve the lymph nodes than carcinoma of other organs, and usually when it does only the regional lymph nodes give evidence of extension.

Bumpus, in a study of carcinoma of the prostate gland, found that about a third of all cases showed metastasis, and that only 11 per cent of these had involvement of the cervical lymph nodes. This means that about one patient out of thirty with carcinoma of the prostate gland will have metastasis in the cervical lymph nodes. Bumpus found that if metastasis occurred, it was in the sacrum and adjacent part of the spine and pelvis in about 25 per cent of the cases. He stated that in suspected cases roentgenograms need be made only of the pelvis, the lumbar spine, and the heads of the femurs.

SIGNIFICANT FACTORS IN THE COURSE AND DIAGNOSIS OF PEPTIC ULCER

ANDREW B. RIVERS

IT has been noted that there is uniformity of the type of person in whom peptic ulcer is prone to develop. This is even more definite in persons in whom recurring ulcers develop following surgical procedures for the cure of gastric or duodenal ulcer. In a previous paper from this department such ulcers were referred to as a recurring type. Certain definite psychic characteristics were reduplicated in practically all the cases. The patients were all of a nervous, high-strung type: intensive and persistent in their activities, relentless in pursuit of whatever they set out to accomplish, they would carry on in spite of obstacles until quite fatigued nervously and physically. They were practically all worriers and given to periods of depression and pessimism. The periodicity and intermittency of symptoms are determined largely by the variability of psychophysiologic influences under which the patients must live. During periods of great emotional strain, or following unusual physical or mental exhaustion, symptoms are likely to reëstablish themselves, or to become definitely intensified if already present. The rapidity with which symptoms arise following some unexpected catastrophe is often remarkable. I have observed instances in which a fully established ulcer syndrome was reëstablished within a few hours after such an experience.

The case presented herewith is illustrative of a number of factors which seem of significance in the diagnosis and course of benign peptic ulcer.

REPORT OF CASE

A man aged thirty-one years first entered the clinic complaining that he had suffered at intervals from right upper ab-

dominal cramps. He smoked and drank alcohol excessively. The symptoms from which he sought relief dated back one year. The pain, which at times was quite severe, usually came on from half an hour to five hours after eating, and persisted for about an hour. The distress originated in the epigastrium and right upper quadrant, and was frequently referred through to the back. Occasionally it was so severe that hypodermics were necessary for relief. Alkalies usually afforded relief. A glass of milk would also help. The pain never came on immediately after eating, and the type of food eaten made little difference.

On general examination slight tenderness was elicited in the right upper abdominal quadrant, and the upper right rectus muscle was spastic. Estimation of gastric acidity showed total acid of 64 and free hydrochloric acid of 48. A few fine food remnants were found in the expressed material; a total amount of 80 c.c. was recovered. Roentgenograms showed duodenal deformity. A diagnosis of duodenal ulcer and possible disease of the gallbladder was made, and operation was advised.

At operation a duodenal ulcer was found. There were many adhesions about the duodenum, suggesting a perforating type of lesion. The gallbladder did not show evidence of disease. The appendix was definitely infected. Appendectomy and posterior gastro-enterostomy were performed. Convalescence was without untoward incident, and for eighteen months after the operation the patient remained well. Then his wife became ill and he came with her to the clinic. He worried about her, and attributed the recurring gastric symptoms to worry incident to her illness. His symptoms at this time were like those he had had prior to his operation. The pain originated in the upper right quadrant and radiated all over the abdomen. It was assumed that the symptoms were due to a reactivated duodenal ulcer. He was put on a milk and alkali regimen, with complete relief of symptoms. Later his son became ill and died, and again he had recurrence of gastric symptoms. For several months he had intermittent spells of indigestion; then after an alcholic excess, he vomited some blood. This incident occurred about four years after the operation. During the following year he had spells of pain oc-

curring daily for a week or so, then a few days of relief. Worry invariably brought on these spells. The pain during this period occasionally became very severe, and he began to observe that the pain originated to the left and slightly below the level of the umbilicus and from there it was referred downward and to the back. Food and soda did not relieve him as consistently as they had previously. Five years after his operation, and one year after the onset of pain in the lower part of the abdomen, he returned to the clinic for another examination. Symptoms had gradually increased in severity, and the periods of relief between exacerbations were becoming shorter. Gastric contents showed a total acidity of 66, free hydrochloric acid of 50, and 300 c.c. of residue. Roentgenograms gave definite evidence of jejunal ulcer. At operation a gastrojejunal ulcer was found, which had almost perforated through into the colon. The duodenal ulcer showed signs of activity. A posterior Polya type of operation was performed. There has been no further evidence of trouble.

This case is an excellent example of the type described. The neurogenic factors seem to be of primary importance in determining the course of a peptic lesion, and may be of primary importance in its development. There seems to be little doubt that the actual period of activity of the ulcer is frequently determined by the fluctuation of these psychophysiologic factors. The intimate physiologic mechanisms set in motion during these periods of nervous unbalance are as yet imperfectly understood, and more must be known about the effect of sympathetic and parasympathetic interaction on gastroduodenal motility and secretion before many of the conditions associated with ulcer can be explained satisfactorily.

I have observed repeatedly that patients on a medical regimen for ulcer seem to make very little progress unless they can become thoroughly relaxed. The adequate reduction of free hydrochloric acid in the gastric content cannot, as a rule, be accomplished if the patient is worried or emotionally disturbed.

An attempt is being made in our department to apply these observations in a practical way in the medical treatment of peptic ulcer. It is practically impossible to change man's tem-

perament, and it is most difficult to keep a man who is a worrier from becoming mentally disturbed during periods of unpleasant experience. It is possible, however, to instruct these patients regarding the importance of evading situations which cause anxiety and which place them under tension. Usually the patient's coöperation is excellent. At the onset of treatment rest in bed is advised in order to obtain as much relaxation as possible. This procedure in itself is frequently sufficient to stop the distress of uncomplicated peptic ulcer. Rather large doses of bromides, phenobarbital, and belladonna are also given to help obtain further rest and relaxation. Much smaller doses of alkalies are then usually sufficient to reduce the gastric acidity sufficiently to permit healing of the ulcer.

Environmental conditions are also significant; pleasant surroundings is a valuable aid in keeping the patients from becoming introspective and dispirited.

In the case reviewed here it is apparent that the examining physician suspected associated disease in the gallbladder, undoubtedly because of the pain in the upper right quadrant of the abdomen. It may be extremely difficult to distinguish this pain from that caused by disease of the gallbladder. Subacute perforating types of duodenal ulcer frequently cause pain in the upper right quadrant of the abdomen. In spite of the fact that the roentgenograms in a series of cases of subacute duodenal ulcer recently studied showed definite duodenal deformity, and the history included the characteristics usually attributed to peptic ulcer, associated disease of the gallbladder was diagnosed in 37 per cent. Exploration for evidence of disease in the gallbladder failed to show the presence of a lesion. It is therefore important in making a differential diagnosis of disease of the gallbladder and peptic ulcer to remember not to place too much significance on the site of the distress. Complete data concerning the history must always be obtained and carefully evaluated, and whenever possible roentgenologic examination should be carried out in cases in which the diagnosis is doubtful.

The pain caused by an infected gallbladder is usually fairly well localized in the upper right quadrant. From this area it is

frequently referred around or through to the back, particularly if pancreatitis is associated. The pain caused by subacute perforating duodenal ulcer may thus far exactly mimic that caused by disease of the gallbladder, but whereas the distress of the gallbladder is frequently further referred into the right shoulder, this rarely occurs in peptic ulcer. Although the pain caused by uncomplicated duodenal ulcer may be referred through to the back, such a symptom usually suggests the possibility of a penetrating type of lesion, particularly if the ulcer has caused bleeding, or if the pain is severe and lancinating. Similarly, pain referred from the epigastrium into the thorax is often diagnostic of this type of complication. It should be mentioned, however, that pylorospasm, whether of an organic or functional type, may cause discomfort in the epigastrium and thorax; it is accompanied ordinarily by flatulence and distention of the upper part of the abdomen without the usual characteristics of the ulcer syndrome.

The pain which is most frequently diagnostic of a perforating peptic lesion starts in a well localized epigastric area, spreads from there upward along either margin of the sternum and then "explodes" into the thorax. The pain of a perforating type of ulcer may simulate closely in character and situation that caused by coronary disease. A patient with perforating gastric ulcer frequently experiences pain in the region of the sternum; this is often mistaken for angina pectoris.

In the case reported here it is apparent that the syndrome established eighteen months after the operation was a reduplication in all details of the preoperative syndrome. The pain was again in the upper right quadrant, and presented the same characteristics as were noted preoperatively. In all probability these symptoms were caused by reactivation of the original lesion in the duodenum. The symptoms were then easily controlled by diet and alkalies. If, following an operation for peptic ulcer, there is reduplication of the preoperative complaints, and if the area of distress is identical in situation and extent, in all probability there is reactivation of the original lesion, or if the ulcer was excised, it is suggestive of a recurring lesion in the same situation.

The development of pain in an area definitely removed from the original site of distress usually argues for a lesion in an area removed some distance from the first lesion. The pain of a jejunal or stomal ulcer is described by the patient as being further to the left and lower than the original complaint. The pain may start in an area about the level of the preoperative complaint, but almost invariably it is then referred downward. The pain of jejunal ulcer is frequently referred through to the back at a level lower than that experienced with the first lesion. Jejunal ulcers are frequently of the perforating type, and this may account for the great number of patients with anastomatic lesions who complain of pain in the back. For this same reason the pain of jejunal ulcers is not so satisfactorily controlled by the ingestion of food or soda.

The perforating type of peptic ulcer responds poorly to a medical regimen and, therefore, such a condition should be recognized before the type of treatment is advised. One of the reasons the nonsurgical treatment of peptic ulcer is so often unsuccessful is that all types of ulcer are submitted to treatment regardless of the histopathologic and anatomic characteristics, or the possibility of associated lesions elsewhere in the gastrointestinal tract.

A duodenal ulcer of the perforating type usually is not greatly benefited by medical treatment, and operation, as a rule, becomes necessary before lasting results can be obtained. If definite symptoms recur following gastro-enterostomy, and if these have the clinical and roentgenologic characteristics of gastrojejunal ulcer, further surgical treatment usually becomes necessary. Lasting benefit has occasionally been obtained by nonsurgical methods in treating inflammatory lesions about the stoma. These lesions, however, were apparently not complicated by obstruction or perforation.

Occasionally indurated areas, with or without the formation of a shallow mucosal ulcer about the stoma, cause definite symptoms, and practically all the clinical and roentgenologic manifestations of jejunal ulcer. These usually respond well to nonsurgical methods of treatment.

A CASE OF DIABETES MELLITUS WITH THROMBO-ANGIITIS OBLITERANS

S. Franklin Adams

A man aged forty-eight years came to the clinic because of a sore on the right great toe of eight months' duration. This sore had discharged a little pus from time to time, and did not show a tendency to heal; in fact, the eroded area was gradually increasing in size and depth. Seven years before he had had phlebitis of the veins of the legs. Fever was noticed at this time, but the swelling, red streaks, and pain persisted for a month or more before the process subsided. There was no further trouble for two years; then the arches began to cause pain. His work as a barber demanded that he stand most of the time, and the prolonged standing was a distinct hardship. He noticed that rest would relieve the pain entirely, but that if he attempted to walk two or three blocks the pain in the arch would return. He was supplied with arch supports, but he was not relieved. About three years before he came to the clinic he noticed that the feet became cold easily, and two years before slight blueness of the left foot and a sore on the great toe were noticed. At this time a physician thought that the left great toe would have to be amputated, but improvement occurred and the operation was not done. At no time during the course of the illness was the patient harassed by intense pain. The patient had begun to smoke at the age of twelve years, and smoked from twenty to thirty cigarettes daily up to the time of examination. Three years before admission he weighed 224 pounds. At that time he suddenly became very thirsty and lost weight. He did not consult a physician, however, for a year and eight months, and then considerable sugar was found in the urine. He was advised to eat food limited in its content of glu-

cose. Insulin was not given until two months before examination at the clinic. When he entered the clinic he was eating food consisting of 90 gm. of carbohydrate, 75 gm. of protein, and 145 gm. of fat, and he was taking 7 units of insulin before breakfast and before supper.

On examination, the patient was still slightly obese. The right great toe was gangrenous. The remaining toes of the right foot were cold and blue, and pulsation could not be felt in the dorsalis pedis or posterior tibial artery. The toes of the left foot were distinctly blue and there was intermitent pulsation of the dorsalis pedis artery. When the feet were elevated for one minute and then lowered, there was a slow return of blood; the return was slower in the right foot. Pulsation was definitely diminished in both popliteal arteries. The pulsation in the femoral arteries and in the arteries of the arms seemed normal. There was weakness of the muscles of the right shoulder, arm, and forearm (crutch palsy). The appearance of the feet did not suggest the usual features of diabetic gangrene and the patient was a little younger than average for that condition.

Daily analysis of the urine did not show any abnormality except occasionally a trace of sugar. The Wassermann reaction of the blood was negative. The blood count was normal. Leukocytosis was not present. The blood urea was 38 mg. for each 100 c.c. The fasting blood sugar did not rise above 198 mg. for each 100 c.c.

A diet consisting of 100 gm. of carbohydrate, 50 gm. of protein, and 170 gm. of fat was given. This kept the urine free from sugar without the use of insulin. Typhoid vaccine was given on five occasions with the hope of improving the circulation in the feet. The systemic reaction produced by the vaccine did not aggravate the diabetic condition. Postural exercises were advised. The patient was dismissed from the clinic. Recently he replied to an inquiry as follows: "I have no pain, the sore is about healed, the feet are warmer. I am continuing with the typhoid vaccine injections. No new sores have developed. My urine is free from sugar."

The features of this case indicate that the patient has oc-

clusive vascular disease. In all probability the process is characteristic of thrombo-angiitis obliterans. The process may be solely on the basis of atherosclerosis, but one would expect to find more definite evidence of sclerosis in such a condition. Furthermore, the process evidently began when the patient was only forty-one years of age. The absence of pain is evidence against thrombo-angiitis obliterans, but the history of phlebitis, then arch claudication pain, and then calf claudication pain are all in favor of it.

The history suggests that the process now taking place in the right foot occurred in the left foot two or three years ago, and that by means of collateral circulation or canalization the circulation of that foot has been reëstablished fairly well. In this event one may look for improvement in the circulation of the right foot with preservation of the leg. For the present prognosis is good because of absence of pain, because of the rather small area of gangrene, because of the slow progression of the disease, and because of the improvement which occurred while the patient was under observation.

FOREIGN BODIES IN THE BRONCHI OVERLOOKED AT BRONCHOSCOPIC EXAMINATION: REPORT OF THREE CASES

PORTER P. VINSON

MANY observers have recorded instances of prolonged suppurative processes in the lung secondary to unsuspected foreign bodies in the bronchi. If such a foreign body is opaque to the roentgen ray, the diagnosis is made apparent by roentgenoscopic examination, and even though the foreign body is in an abscess cavity beyond a bronchial stricture and cannot be visualized through a bronchoscope, it is usually possible to remove it under fluoroscopic guidance. However, if the history of aspiration is questionable, if the foreign body is not opaque to the roentgen ray and is situated distally to a stricture of the bronchus, and beyond the point of vision, the difficulties of diagnosis and removal become apparent.

It must be borne in mind that there are many pulmonary abscesses of uncertain origin, and in every such case the possibility of a foreign body, nonopaque to the roentgen ray, must be suspected as an etiologic factor, and every effort should be made to locate and remove it.

In most instances the foreign body can be found and removed, but the following three cases serve to show that bronchoscopic extraction is not always possible, although the bronchoscopic dilatation of the bronchial stricture was unquestionably an aid in the spontaneous expulsion of the foreign body in two of the cases.

Case 1.—A man aged sixty-nine years was examined April 6, 1922. He had been quite well until December, 1921, when he choked while eating chicken soup. He thought he had as-

pirated a bone. Following this he had had much cough with purulent sputum, chills, and fever.

General examination and roentgenoscopic examination of the thorax did not reveal abnormality. Bronchoscopic examination was made April 24, 1922; a granuloma was found and removed from the anterior wall of the bronchus to the right lower lobe. This granuloma contained a piece of bone 2 by 1 mm. Another bronchoscopic examination was made May 5, 1922, and nothing was found. The patient was quite well, save for a little cough, until June, 1926, when the cough became worse, expectoration increased in amount and he again began to have fever. He returned for reconsideration August 10, 1926. The breath sounds were distant at the base of the right lung and resonance was impaired over the same area. Roentgenologic examination of the thorax revealed an area of bronchiectasis at the base of the right lung.

Bronchoscopic examination was again performed August 17, 1926, and a large amount of pus and granulation tissue was found in the bronchus leading to the lower lobe of the right lung. The pus was aspirated and granulation tissue which was removed with forceps was found to contain small pieces of bone. After this tissue was removed an abscess cavity was entered and a considerable amount of creamy, purulent material was aspirated.

Another bronchoscopic examination was done September 9, 1926, when the aspirator was passed through the area of stenosis in the bronchus, a foreign body was felt, and several small pieces of bone were removed. The patient coughed out a large piece of bone September 19, and since then he has been perfectly well.

Case 2.—A man aged thirty-three years was examined February 5, 1923. He had been well until September, 1921, when a cold with fever had developed. Following this he had had cough with some expectoration, that was particularly troublesome at night. In November, 1921, the sputum had become bloody and the patient was thought to have pulmonary tuberculosis, although the sputum did not contain bacilli of tuber-

culosis. Roentgenologic examination of the thorax had revealed increased density, presumably at the base of the left lung. Bronchoscopic examination had been made and the patient had been told there was an ulcerated bleeding area on the wall of the trachea. His condition had remained about the same until January, 1923, when, following an acute infection in the throat, his heart became rapid and he lost about 12 pounds in weight in spite of a good appetite.

The observations on general examination suggested that the patient was suffering from an exophthalmic goiter, and determination of the basal metabolic rate showed it to be +40 per cent. The observations on examination of the thorax were not significant, but a roentgenogram of the thorax showed the heart to be slightly enlarged and drawn to the left, probably the result of chronic infection of the pleura. Although the patient was nervous and had a rapid pulse, it was decided to examine the trachea bronchoscopically because of the observations at the bronchoscopic examination elsewhere. The examination was done as hurriedly as possible, and there was no evidence of a lesion in the trachea. Purulent secretion was seen in the bronchi, especially on the right side, but further examination was not made. February 23, 1923, a portion of a parenchymatous hypertrophic thyroid gland was removed under local anesthesia and the following day there was an elevation in temperature to 102° F. This fever persisted, and March 3, aspiration at the base of the left lung yielded a few drops of yellow pus. The empyema cavity was drained through a catheter. Following the initial drainage the patient improved in every way and a slight nonproductive cough was the only residual symptom.

In November, 1923, the patient experienced a rather severe paroxysm of coughing and ejected a portion of a tooth from the lung. Although it was necessary to perform several plastic operations on the empyema cavity, complete healing occurred in a year from the onset of the acute illness. Even after the foreign body had been expelled from the lung the patient did not remember having had any dental work done preceding the original illness.

Case 3.—A woman was examined June 24, 1929. She had not been well for about five years, having suffered considerably from tonsillitis, quinsy, and periods of general weakness. In July, 1928, she had had a spell of weakness; her physician had told her she had a goiter and he gave her iodine. In September, 1928, the upper teeth were extracted, and although she had had some cough before this, it became worse, but was not accom-

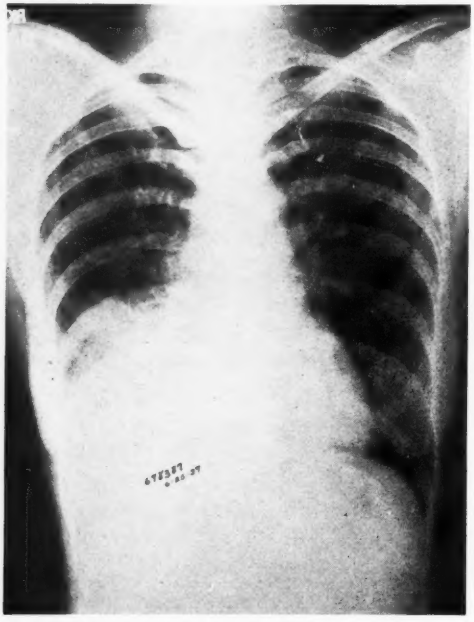

Fig. 129.—Case 3. Infiltration of the lower lobe of the right lung.

panied with expectoration. In December she had influenza, but was quite normal after a week, and save for periods of weakness, she was fairly well until five weeks before coming for examination, when a severe cold developed that was soon followed by cough, fever, purulent sputum, and loss of weight.

On examination it was found that the patient had an exophthalmic goiter, with a basal metabolic rate of +57 per cent,

and an abscess in the lower lobe of the right lung (Fig. 129). Bronchoscopic examination, July 5, 1929, revealed extensive suppuration in the lower lobe of the right lung with pus exuding from many bronchi. The bronchi were thoroughly dilated and aspirated. A foreign body could not be seen.

Bronchoscopic examination was repeated August 28, 1929, with the same observations as at the previous examination.

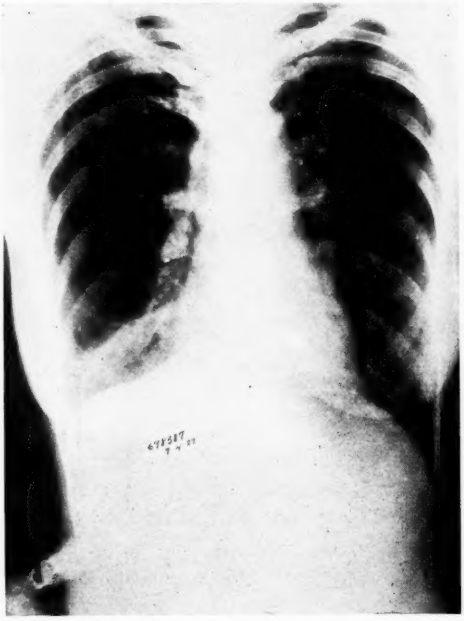

Fig. 130.—Case 3. Two months after bronchoscopic aspiration.

Following the first bronchoscopic examination there was marked improvement in the general condition of the patient, with considerable gain in weight and strength and a remarkable resolution in the pulmonary lesion (Fig. 130).

September 10, 1929, the goiter was removed without untoward reaction. After the patient's return home she continued to cough, and November 1, 1929, she expelled a piece of bone

that had evidently been aspirated at the time her teeth were extracted a year previously (Fig. 131).

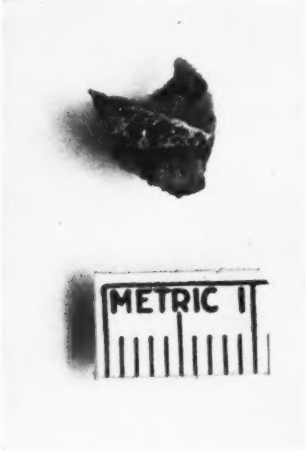

Fig. 131.—Case 3. Foreign body spontaneously expelled from the bronchus.

FURTHER OBSERVATIONS ON CHRONIC ULCERATIVE COLITIS ASSOCIATED WITH SPLENOMEGALY

J. Arnold Bargen and Herbert Z. Giffin

In the last Mayo Clinic issue of *Medical Clinics of North America* we reported[2] a case of long-standing chronic ulcerative colitis in which marked and progressive splenomegaly developed. This paper is a presentation of other cases which seem to demonstrate more than an incidental relationship between chronic ulcerative colitis and a syndrome which might be confused with splenic anemia.

One of us (Giffin) in 1913, separated certain cases simulating splenic anemia into a group classified as "chronic infectious splenomegaly" and Wilson reported on the pathologic condition of removed spleens. In these cases there was a history of recurrent furunculosis, chronic recurring endocarditis, arthritis, and peripheral, mesenteric or portal thrombosis; in 1927[6] chronic ulcerative colitis was recognized as a causative factor in chronic infectious splenomegaly.

The literature of the subject was considered in our former paper, but it may be well to mention the work of Sbrocchi, Frugoni, and Chabrol and Binard on intra-abdominal thrombosis because of a probable relationship of ulcerative colitis, thrombosis, and splenomegaly.

The occurrence of diarrhea in our earlier cases of splenic anemia and the demonstration of actual colitis in later cases has led to the conviction that this association between colitis and splenomegaly is not rare.

Case 1.—A boy, aged fifteen years, came to the clinic in June, 1928, with a four-year history of dysentery associated with the passage of blood; he passed an average of twelve stools

a day. Two years prior to admission, his physician had recognized enlargement of the liver.

At the time of examination the patient was found to be anemic and sallow. His weight had been 117 pounds and was then 102. The temperature was 99.2° F. in the afternoon. In the left upper quadrant of the abdomen a large movable, firm mass, moving with respiration, thought to be the spleen, was palpable. Its lower margin descended to the level of the iliac crest. The hemoglobin was 40 per cent; erythrocytes numbered 2,390,000, and leukocytes 7,200, of which 69.5 per cent were polymorphonuclear neutrophils. Urinalysis was negative; parasites, ova, or acid-fast bacilli were not found in the stools; the Wassermann reaction of the blood was negative; serum bilirubin and fragility of the erythrocytes were within normal limits. A roentgenogram of the colon by barium enema showed the deformity of chronic ulcerative colitis of the entire colon. The proctoscopic examination revealed chronic ulcerative colitis, graded 2, with a ring stricture, less than 1 cm. in diameter, 7 cm. from the anus; scrapings from ulcers in the rectum did not reveal acid-fast bacilli. Splenectomy was considered but it was thought best to treat the severe colitis first and observe the effect on the spleen. The patient did not improve satisfactorily on the usual treatment. August 9, acute left lower abdominal pain with increased bleeding by rectum occurred and examination showed a tender sausage-shaped mass in the left lower quadrant along the line of the colon. It was noticed at this time that the spleen was not quite half the size it had been on admission. A diagnosis of subacute perforation was made and operation was advised. August 12, ileostomy was performed. After a stormy course the patient died, August 27.

The postmortem observations were as follows: Generalized peritonitis, splenomegaly, hypertrophic juvenile cirrhosis of the liver (weight 1,185 gm.), and perisigmoidal inflammatory mass with extensive chronic ulcerative colitis. The spleen weighed 537 gm.; it was 17.5 by 9.5 by 5.5 cm., and grayish-blue. Its capsule was thickened. Surfaces made by sectioning appeared "meaty" and grayish-pink. The microscopic examination re-

vealed an enormous increase in fibrous tissue, the sinusoids were dilated and only a few small collections of lymphoid cells were seen. The pathologic diagnosis was chronic splenitis and perisplenitis, marked interstitial fibrosis, and destruction of pulp, dilatation of sinusoids, and almost complete destruction of malpighian bodies.

Case 2.—A girl, aged six and a half years, was brought to the clinic March 8, 1926. She had had intermittent attacks of diarrhea for four years. She had done fairly well on symptomatic treatment, consisting of a proprietary powder and regulation of diet, until August, 1923, when she began to pass bloody stools, with mucus; an average of twenty-four stools were passed in twenty-four hours. In November, 1923, tonsillectomy was performed without effect on the bowels. In December the hemoglobin was 30 per cent. January 20, 1926, she was given 500 c.c. of blood intravenously. Early in February a persistent fever appeared, ranging between 102° and 106° F., and this condition had persisted until she came to the clinic.

The child was much undernourished, and was passing an average of ten or twelve bowel movements a day. Proctoscopic examination showed the typical picture of chronic ulcerative colitis and the roentgenogram of the colon demonstrated narrowing, and foreshortening. In the left upper quadrant of the abdomen there was a smooth tumor with a definite rounded edge, moving with respiration, the lower margin of which at rest was at the level of the umbilicus, corresponding to the position of an enlarged speen. Fever during the first two weeks was of a typical septic type, normal in the morning and 103° to 104° F. in the afternoon. Every time the patient ate, her bowels would move. Her weight was 35 pounds. The third week her temperature did not exceed 100° F. The fourth week it reached 102° F. She was given autogenous vaccine prepared from the diplococcus isolated from the ulcers in the rectum. The hemoglobin on admission had been 40 per cent, with 3,170,000 erythrocytes for each cubic millimeter. May 4 it was 70 per cent, with 4,200,000 erythrocytes. She gradually improved and was dismissed May

14; the temperature was normal, and at this time she was receiving 0.7 c.c. of vaccine subcutaneously. She got along fairly well during the summer, but in the latter part of August had a relapse. She returned September 12, at which time the hemoglobin was 60 per cent and the leukocytes numbered 19,200. At the previous visit they had ranged between 6,000 and 9,200. The spleen, which was enlarged to the level of the umbilicus at the first visit, could not be felt. Except for several remissions, during which she seemed better for a week or a few days at a time, there was a steady decline so that February 12, 1927, the hemoglobin was 20 per cent, and erythrocytes numbered 1,610,000. Preceding and following this, she was given repeated transfusions of blood.

February 9, 10, and 12, the patient was given 5, 15, and 10 c.c., respectively, of the immune serum. High fever was present and later severe urticaria. There was slight immediate response so that for five days, from February 16 to 21, the temperature ranged around 99° F. and the stools were fewer. Following this the fever and the bleeding recurred. From February 21 to March 3, the hemoglobin ranged around 30 per cent. Ileostomy was done March 2, and death occurred the next day from peritonitis.

At necropsy, the spleen was not greatly enlarged, but it was large for the size of the patient. It was nodular and reddish-purple, and the malpighian corpuscles were enlarged. There was splenitis with marked leukocytosis, and lymphocytic infiltration of the pulp with hyperplasia of the malpighian bodies.

It is noteworthy that in these two cases, as well as in the cases reported previously, the disease began in early childhood, was very severe, and ran a long protracted course with numerous severe exacerbations and slow progression. In Case 1 of this series there was marked fibrosis and evidence of chronic infection. In Case 2 it will be noted that whereas at one examination the spleen was large, the enlargement had receded during the time of partial remission, but in spite of this there was definite evidence of hypertrophy; the pathologic picture was that of subacute splenitis.

Case 3.—A man, aged forty-two years, came to the clinic in July, 1925, stating that two years prior to admission, he had begun to have rectal bleeding with diarrhea, and since then the stools had been loose. About January, 1925, he had begun to notice general weakness, and pallor. During the two years his weight had dropped from 194 to 148 pounds. He frequently had had night sweats, with chills and fever, in the last six months.

On admission the patient was pale and fairly well nourished; the temperature was 98.4° F. There was dulness in both upper quadrants, and the liver and spleen were enlarged, although the edge of the spleen was not felt. The hemoglobin was 33 per cent; the erythrocytes numbered 3,830,000, and the leukocytes 8,600, of which 71.8 per cent were polymorphonuclear neutrophils. Gastric analysis, the Wassermann reaction of the blood, two examinations of the stools for parasites and ova, clinical and roentgenologic examination of the thorax and roentgenogram of the stomach were all negative. The colon above the brim of the pelvis was normal by roentgenogram. Proctoscopic examination revealed evidence of healing chronic ulcerative colitis. A diagnosis of splenic anemia was considered but the infectious element was prominent and the spleen was not markedly enlarged.

This is a different type of case, for here the colitis was mild, apparently began in adult life, had not progressed extensively, and yet anemia was marked. The possibility of two entities might be entertained, that is, splenic anemia and chronic ulcerative colitis, but in view of other experiences with splenomegaly and infectious disease, it seemed best to place the case in the group of infectious splenomegaly.

Case 4.—A woman, aged thirty years, came to the clinic in April, 1924, with a history of diarrhea, abdominal pain, and distention of five years' duration. Her trouble began with an attack of what was believed to be influenza in 1919 when she had been in bed for six weeks. While in bed she began to have attacks of acute epigastric pain associated with nausea, vomiting, and diarrhea. At first there were only two or three watery stools

mixed with mucus in twenty-four hours, but the number of stools gradually increased. The condition continued for about a year and a half. When improvement began, she gained 25 pounds in weight until the winter of 1923, at which time she was confined to bed for eight weeks on account of bronchopneumonia. During this sickness the symptoms referable to the bowel returned, and about this time a tumor in the region of the spleen was first noted, which gradually increased in size. She was passing from eight to ten bloody, foul-smelling rectal discharges and in the year prior to admission, she lost 25 pounds in weight. As far as she knew, chills or fever had not occurred.

The patient was small and pale, and had a hacking cough. The edge of the liver was smooth and rounded. The tumor, which seemed to correspond to the spleen, extended to the median line and to the level of the iliac crest, moving with respiration. The hemoglobin was 43 per cent; the erythrocytes numbered 3,180,000, and the leukocytes 5,000, of which 74 per cent were polymorphonuclear neutrophils. There were purpuric spots on the thighs and knees; the tourinquet test gave positive results. Blood platelets numbered 94,000; coagulation time (Bogg's) was five minutes and bleeding time three and a half minutes. The purpura was mild and was regarded as a secondary infectious condition. Repeated examination of the sputum did not show acid-fast bacilli; the Wassermann reaction of the blood was negative; the erythrocytes showed increased resistance. Roentgenograms of the thorax, kidneys, ureters, and bladder were negative. Roentgenologic examination of the colon by barium enema showed the deformity of chronic ulcerative colitis of the entire colon. The proctoscope revealed the usual picture of chronic ulcerative colitis. There were six teeth with periapical infection and the tonsils were infected. Complete investigation with provocative tests was entirely negative for syphilis. It seemed definite that splenomegaly was advancing with the development of ulcerative colitis, and the clinical picture was that of low-grade chronic sepsis. Splenectomy was considered, but was abandoned for the time.

The striking feature in this case was the marked splenomegaly

with the relatively less severe colitis. Here, too, the disease began in early adult life and although clinically not severe, involvement of the colon was extensive, anemia was marked, and another striking feature was the onset of both of the exacerbations with severe respiratory infections, on one occasion severe influenza, and on the other bronchopneumonia.

Case 5.—A man, aged fifty-one years, came to the clinic in March, 1923, complaining of a tumor in the left side of the abdomen and of diarrhea. Three years prior to admission, with the first cold weather, diarrhea developed, with the passage of blood and mucus. Some days stools passed hourly. This continued throughout the winter, and the following summer he improved somewhat. In September, however, a similar condition occurred, this time with abdominal cramps. Examination by a physician elsewhere disclosed a mass in the left side of the abdomen. His condition continued about the same until admission to the clinic. Treatment had consisted of irrigations of hot water at a temperature of 127° F.

The patient's physical condition was fairly good. He weighed about 170 pounds. The tumor, which was thought to be the spleen, filled the left side of the abdomen, extending to the umbilicus and to the iliac crest. One urinalysis did not show albumin; two subsequent urinalyses showed albumin graded 2 and 3, but there were no other indications of renal disease. The hemoglobin was 74 per cent; erythrocytes numbered 4,970,000, and leukocytes 7,400, of which 65.5 per cent were polymorphonuclear neutrophils. Test of fragility of erythrocytes was negative; the coagulation time and bleeding time were normal. Proctoscopic examination revealed extensive chronic ulcerative colitis with marked activity. High in the rectum were two small polyps. The roentgenogram of the colon by barium enema showed deformity of chronic ulcerative colitis of the left half of the colon. Cystoscopic examination indicated that the mass of the left side of the abdomen was extrarenal. A roentgenogram of the thorax, two cultures of the blood and the Wassermann reaction of the blood were negative.

Septic splenomegaly associated with colitis was diagnosed, and splenectomy was suggested because of the marked enlargement of the spleen and the patient's good general condition, but the patient decided to delay such an operation. He returned in December, 1924. He had had a fair year; he had passed an average of only six to seven stools a day during the summer, but three months before admission he had slowly become worse. At this time, in addition to the large spleen, there were ascites and edema of the legs. The serum bilirubin was 3.5 mg. for each 100 c.c. Hemoglobin was 59 per cent; erythrocytes numbered 3,650,000 and leukocytes 4,600, of which 71 per cent were polymorphonuclear neutrophils. Proctoscopic examination showed the condition to be about the same except that there were numerous sessile polyps in the rectum. During the month of his stay in the hospital he did not improve, and was allowed to return home the middle of January. Death was reported later without date.

The seriousness of the condition in this case, as based on the features associated with the splenomegaly, rather than with the colitis, is noteworthy. That the two conditions developed in association can hardly be questioned. For future treatment in other cases it becomes difficult to decide which feature of this combination of conditions necessitates greater emphasis; the subsequent history indicates that the decision for splenectomy was justified.

Before the diagnosis of chronic ulcerative colitis became well established and before we had such definite diagnostic data, there were observed at the clinic several cases of splenomegaly associated with diarrhea of a type which in retrospect at least lends suspicion that these cases, too, may have been cases of chronic ulcerative colitis. We are reporting them merely for the purpose of inciting suspicion, in any case of longstanding dysentery with splenomegaly, that there may be a relation between this infectious type of colitis and the splenic enlargement. We believe this is particularly opportune in the light of a recent report of Seeber and Spröhnle. They reported the case of a patient, aged thirty-nine years, who was under observation at intervals

in the same clinic for twenty-seven years. His trouble started at the age of twelve, in 1901, with acute dysentery associated with the passage of blood, and severe abdominal pain, confining him to bed for three weeks. He had recurrent attacks of dysentery, the second one in 1906 when he was confined to bed for nine weeks. Splenomegaly was noted at the first admission. The patient died in 1928 and the pathologist, in his report on the spleen, made note of its size, the fibrous calcareous regions, the markedly thickened trabeculae and the lymphocytic and plasma-cell infiltration. This case raises the question of a relation between the condition in the bowel and splenomegaly.

Case 6.—A boy, aged four years, was brought to the clinic December 1, 1910. The complaint was of gradually increasing enlargement in the left upper quadrant of the abdomen of two years' duration. There had been spells of diarrhea at intervals, lasting three or four days, and three months before admission, there had been severe diarrhea, fever, and pain in the abdomen of three weeks' duration. On admission the bowels were quite regular, the stools were large, and the abdomen was somewhat distended. The enlargement was identified as spleen. The hemoglobin was 65 per cent; erythrocytes numbered 3,970,000, and leukocytes 3,050, of which 44 per cent were small lymphocytes, 11 per cent large lymphocytes, 43 per cent polymorphonuclears, 1 per cent eosinophils and 1 per cent transitionals. There is no record that the patient has died.

Case 7.—A man, aged forty-nine years, came to the clinic in June, 1912, saying that he had never been strong, and that his stools had been bloody since the age of fifteen years. Two years prior to admission there had been a severe pain in the left subcostal region which had continued for several months, at which time a physician had found a tumor in the left upper quadrant of the abdomen. He had lost 20 pounds in weight. The tumor, which was thought to be the spleen, descended to the level of the iliac crest. The hemoglobin was 45 per cent; erythrocytes numbered 5,080,000, and leukocytes 5,500, of which 30 per cent

were small lymphocytes, 9.7 per cent large lymphocytes, 57 per cent polymorphonuclears, 0.7 per cent transitionals, 1.7 per cent eosinophils, and 0.7 per cent basophils. A diagnosis of splenic anemia was made at that time. The spleen was removed July 5, 1912.

The spleen measured 30 by 25 cm. and weighed 1,000 gm.; the exterior was smooth and soft; the surfaces made by cutting were smooth, soft, and dark colored; the lymphoid tissue was markedly hyperplastic, and there was some swelling of the endothelium of the venous sinusoids and capillaries, which were dilated; there was marked connective-tissue overgrowth.

The patient died in January, 1916; cause of death not known.

Case 8.—A woman, aged fifty years, came to the clinic in June, 1910. She had had typhoid fever at the age of thirteen years, and inflammatory rheumatism two years prior to admission. In October, 1909, she had begun to have diarrhea without visible blood or mucus. Her bowels would move after each meal. Prior to this time she had been constipated. The patient had lost 25 or 30 pounds in the two years before admission. Two months before admission a tumor had been found in the abdomen; this tumor, which corresponded to the spleen, extended below the level of the left iliac crest. Many of the joints were enlarged from old arthritis. The hemoglobin was 50 per cent; erythrocytes numbered 4,550,000, and leukocytes 1,000, of which 62 per cent were lymphocytes, 30 per cent polymorphonuclears, 5 per cent transitionals, 2 per cent basophils, and 1 per cent myelocytes. Exploration was undertaken July 11, 1910; the spleen was removed.

The weight of the spleen was 1,385 gm.; it measured 30 cm. in length; the exterior surface was smooth and soft; a surface made by cutting was smooth, mottled, soft, and dark colored; the lymphoid tissue was greatly increased in amount; there was considerable endothelial proliferation in venous sinusoids and dilated capillaries were visible; the connective tissue was increased in amount.

The patient died August 29, 1921.

Case 9.—A woman, aged forty-nine years, came to the clinic in May, 1908, complaining of a tumor in the left side of the abdomen, which had first been noted nine months previously, and diarrhea, with considerable bleeding, which had been present for a year. The family history was inconsequential. Examination showed the spleen to descend below the level of the left iliac crest. The hemoglobin was 70 per cent; erythrocytes numbered 2,840,000, and leukocytes 6,500. Exploration, July 2, 1908, revealed a spleen filling the entire left side of the abdomen.

The spleen weighed 1,450 gm.; the exterior was slightly roughened; a surface made by cutting was tough and firm; the lymphoid tissue was increased; there was some swelling of the endothelium of the sinusoids, and marked increase of connective tissue.

The patient died in May, 1911.

COMMENT

In most of these cases chronic ulcerative colitis had been present for a long time. This probably was a factor in the origin of the splenomegaly. Through what mechanism it occurs remains a mystery, for why splenomegaly develops in certain cases of colitis and not in most cases is not known. In a consideration of duration, recurrence and chronicity in this group of cases, it has been found that clinicians have observed approximately eighty times as many cases in which splenomegaly was not noted. In many of the patients with ulcerative colitis the disease has been of much longer duration and recurrent attacks have been more common than in the nine reported cases. Hence, the theory that has been advanced in relation to splenomegaly, that is, that recurrence and duration of disease are primary factors in the splenomegaly, is not fully corroborated.

The fact that in some of these cases splenic enlargement seemed to keep pace with advancement of disease suggests the possible need of the splenic elements in combating the infection; as destruction of the spleen was continued by the constant or recurrent disease, replacement by fibrous tissue and increase in

size resulted. The possible existence of portal or splenic thrombosis or thrombophlebitis secondary to colitis must also be entertained. There must be overwhelming absorption of the infecing organism or its toxin by the immediate colonic circulation; hence mild, partial, or intermittent venous thrombosis is readily conceivable. Finally, the facts lead to the supposition that certain bacteria, whether the primary organisms or secondary invaders, have an affinity for the spleen.

The cases herewith reported show three features which may serve to at least partially distinguish them from cases of splenic anemia and Banti's disease: Leukopenia was absent; the number of leukocytes was usually normal or slightly increased; there were no severe gastro-intestinal hemorrhages, and in spite of the marked splenomegaly the presence of ascites was not demonstrated.

A case of chronic ulcerative colitis with marked splenomegaly, coming under observation during a latent period so far as the colitis is concerned, might logically be considered a case of splenic anemia, but experience suggests that when a history of chronic infection is obtained, splenectomy may be followed by an exacerbation of the infection and at best eliminates only a small portion of the infection and probably a portion of only secondary importance. Most of our patients in whom splenectomy was performed for chronic infectious splenomegaly have later died with nephritis.

It is imperative that this group of cases be separated, if possible, from the group classified as splenic anemia preceding a decision for splenectomy. Only occasionally will splenectomy be indicated in cases of chronic infectious splenomegaly.

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MESENTERIC LYMPHADENITIS IN ADULTS, A CAUSE OF PSEUDO-APPENDICITIS, INDIGESTION, DIARRHEA, AND ARTHRITIS

WALTER C. ALVAREZ

EVERY physician of experience sees from day to day patients with abdominal pain and symptoms of indigestion so severe that he has little doubt about the presence of definite organic disease. When a sensible, well-balanced man or woman wakes out of a sound sleep with pain and nausea, when for days afterward the abdomen remains sore, and when with all this there is a slight, but definite fever, one cannot dismiss the subject with the words "nervous indigestion"; there must be something wrong in the abdomen. But where is it?

The symptoms may suggest the presence of cholecystitis, peptic ulcer, or appendicitis, but often the syndrome is atypical; roentgenograms fail to show disease, and a satisfying diagnosis cannot be made. Often it cannot be made even after careful exploration of the abdomen. The appendix or the gallbladder may be removed, but the pathologist does not find much wrong, and even when the patient improves, the physician who is honest with himself and desirous for real knowledge is left with the feeling that the problem has not been solved.

Such doubts arise not infrequently when one is dealing with children. Almost every symptom and sign will point sometimes to the presence of acute appendicitis and yet when the abdomen is opened the surgeon is embarrassed to find no sign of disease.

As time goes on we physicians must learn more about these puzzling cases. For some of them we will have to get new labels, but for others we can perhaps use labels that are already available, but which as yet are not well known. The particular label to which I wish now to call attention is that of "mesenteric

lymphadenitis." If in the puzzling cases of "pseudo-appendicitis" mentioned in the preceding paragraph the surgeon would always look carefully at the mesentery of the lower part of the ileum he not infrequently would find there a remarkable enlargement of the lymph nodes.

There are reasons for believing that the intestinal mucosa is more permeable in childhood than in adult life. According to Adami bacteria are constantly passing through the wall of the bowel; the lymphatics of the mesentery are always infected, and the nodes near the spine constitute one of the most important lines of defense. This bacterial invasion appears to be most active in the lower end of the ileum and in the cecum, probably because in this region the intestinal contents contain more living bacteria than they do in any other part of the bowel.

For many years mesenteric lymphadenitis has been well known to pediatricians who generally speak of it as tabes mesenterica or mesaraica. More recently there have appeared a number of articles dealing with the syndrome as it appears in adults. It was the excellent paper by Freeman which stimulated me to report some of the cases that I have seen.

Case 1.—A woman, aged twenty-nine years, was first seen in August, 1922, complaining of weakness, loss of weight, abdominal pain, diarrhea, and extreme nervousness. As a child she suffered with sick headaches. Later she had two severe attacks of "grippe." With one she was in bed for three weeks with fever, cough, and uncontrollable vomiting. So far as she knew she had never been exposed to tuberculosis.

Two years before I saw the patient she noticed a tendency to diarrhea and after a time this became troublesome. Her weight which had been 105 pounds dropped to 90 pounds. She noticed slight fever in the afternoons, sometimes as high as 37.8° C. Five months before I saw her there were several attacks characterized by soreness in the muscles, fever, malaise, nausea, cramps in various parts of the abdomen, enlargement of lymph nodes, and changes in the skin which, from the description, represented either erythema nodosum, or giant urticaria. The eyelids were

sometimes badly swollen, the nasal mucosa was often turgid and the voice husky. This suggested an allergic reaction and inquiry showed that she had several asthmatic relatives. She did not, however, show any sign of hay fever or hives during the years in which I knew her. The attacks sometimes preceded menstruation and sometimes started suddenly with epigastric pain which occasionally radiated to the rectum. There was a little dyspnea and the ankles swelled during the day. Menstruation was irregular, and the flow excessive; she sometimes menstruated twice in a month.

General examination showed a small, dark, sallow woman. The lungs appeared to be normal. The temperature was 37.6° C. The abdomen was very tender everywhere. The uterus was large and retroverted. The patient was so nervous that she could not lie quiet on the examining table. Roentgen-ray examination of the lungs showed a little thickening of the shadows about the hilum, but the apexes were clear. Gastric peristalsis was extremely active; the colon was normal. Examination of the stools showed cysts of *Entamoeba coli*.

During the following month in spite of rest in bed the patient continued to have fever of about 37.8° C. She had so little appetite and so much nausea that it was hard to feed her. The abdominal pain subsided. From time to time the nodes in the neck became swollen. The pulse was so fast that hyperthyroidism was thought of but it could not be demonstrated. Blood cultures remained sterile.

During the following year the patient spent most of the time in bed, but she continued to have fever and it was impossible to make her gain much weight. She was unable to do any housework. Sometimes the right thigh and leg became swollen. Urination was very frequent day and night, but no explanation could be found for the irritability of the bladder.

In October, 1922, excessive menstruation associated every month with a flare-up of the fever led to the suspicion that much of the trouble might be due to tuberculous salpingitis, and operation was performed. The uterus was large, red, and boggy; the tubes were normal. Exploration showed some enlargement

of the spleen and much enlargement of all the nodes in the mesentery. There was no caseation and nothing to suggest tuberculosis.

Suspension of the uterus greatly relieved the menstrual difficulties and the patient began to improve. By August, 1924, the fever had gone. Digestion was better, but the abdomen was still sore. In January, 1930, she wrote that she is much stronger; she still has much soreness through the bowels and every four or five months she has an attack during which she vomits everything she eats. She has not had fever for a long time.

To sum up: A frail little nervous woman for years has suffered with a low-grade infection in the lymph nodes of the abdomen and sometimes of other parts of the body. After years of treatment similar to that employed in cases of tuberculosis she recovered.

Case 2.—An unmarried woman, aged twenty-five years, was seen in 1924. She had been well until the age of fourteen years when she remembers having suffered a severe attack of vomiting. There was no pain. For six years following this attack her health was poor; she was weak, she had poor appetite, she lost weight, and she became anemic. Later she suffered with a dull ache in the lower part of the abdomen which came in attacks lasting several hours. The abdomen was always distended at these times, and much flatus was passed. These symptoms grew worse and in the two years before I saw her she had many spells of severe pain in the lower middle abdomen. It doubled her up, and each time the abdomen was sore for days afterward. The soreness was so great that she could not lie prone. Later she began to have distress about 11 o'clock in the morning or in the evening after dinner. She sometimes was nauseated but she never vomited. Menstruation was always scanty, and leukorrhea appeared immediately after one of the acute attacks of abdominal pain.

Examination showed a finely built, well-nourished young woman with a tender liver. Roentgenograms showed a normal stomach and colon, and large calcified nodes to the right of the spine.

On account of the severity of the attacks of pain and the increasing invalidism it was thought best to explore the abdomen and to remove the appendix. At operation all the abdominal organs appeared to be normal and all that could be found to explain the symptoms were the large calcified possibly tuberculous nodes in the mesentery of the lower part of the ileum. The spleen was not enlarged. After removal of the appendix and a few of the larger nodes the patient continued for a time to have much distress and bloating immediately after meals. Constipation, however, was relieved and she gained 10 pounds in weight. For a while there was some anemia.

In January, 1930, the patient wrote that except for some anemia and some tendency to indigestion she had been well.

Case 3.—A tall thin boy, aged seventeen years, was first seen in November, 1922. He had never been strong; as a baby his digestion was bad and later he had severe bronchitis. At the age of eleven years, what was probably a normal appendix was removed. At the age of twelve years, he was in bed for nine months with fever which must have been tuberculous in origin because at the time his elder brother was seriously ill with this disease. There never was any cough, but on several occasions he suffered with pleuritic pain, and for years afterward there was a tendency to fever in the afternoons. Shortly after recovery from this illness the bowels began to be loose, usually in the morning. When I first saw him he was complaining of pain and soreness about the navel, occasional diarrhea, bloating, nausea, heartburn, headache, and attacks of paroxysmal tachycardia.

Examination showed harsh breath sounds over the left upper lobe, but never any râles. Roentgenograms of the thorax showed small shadows which were interpreted as due to healed tuberculosis. Aside from marked spasm at the cardia the stomach was normal; the colon also appeared to be normal. There were no parasites or ova in the stools and the bacterial flora was not distinctly abnormal.

A diagnosis was made of smouldering tuberculosis of the mesenteric lymph nodes and the boy was kept in bed or other-

wise at rest for months. Unfortunately there was not much improvement; the diarrhea was not easily controlled, and when it decreased the flatulence which took its place was even more annoying to the patient.

In February, 1923, the diarrhea was better, but the boy began to have pain in the region of the gallbladder, and the paroxysms of tachycardia became more and more troublesome. In January, 1924, he had an attack of what appeared to be gallbladder colic; it put him to bed for two days with a fever of 38° C. In November, 1924, he had another severe colic, with pain running back under the right shoulder blade, and by April, 1925, these symptoms were so troublesome that he was operated on. The gallbladder and liver appeared to be normal, but all the lymph nodes in the abdomen were much enlarged, particularly in the ileocecal region. The cecum and colon appeared to be normal; the spleen was only slightly enlarged. One of the nodes was removed, sectioned, and put through a Rosenow press. Tubercles could not be found and bacteria were not grown from the juice. The patient continued to have attacks of diarrhea, paroxysmal tachycardia, and soreness about the liver, but he improved in strength and finally was able to go back to school.

In this case the assumption must be that the primary cause of the disease was tuberculosis, but in all the time that others and I have studied the boy we could not prove it. As a number of writers have pointed out, one might have to examine histologically many of the mesenteric nodes before finding one with definite tuberculous changes in it. I have seen a few other cases like this in which smouldering tuberculosis was the only demonstrable cause for a clinical picture of cholecystitis.

Case 4.—An unmarried woman, aged twenty-four years, complained of a smothering feeling in the thorax. At the age of eleven years she was operated on for what was thought to be appendicitis, but instead the surgeon found a number of caseated and calcified lymph nodes in the mesentery. So far as she knows she was never exposed to tuberculosis. She was better for two and a half years after the operation and then had a sudden attack

of severe cramps in the lower part of the abdomen. With the cramps there was violent vomiting and some diarrhea. The attack lasted three days. After this, except for one attack of vomiting and abdominal pain, and occasional nausea and diarrhea, her digestion was good. Four years before her examination a diagnosis had been made of synovitis in both ankles. After this passed off she was well until two months before I saw her. She then suffered severe sharp pain in the lower right quadrant of the abdomen. This kept her in bed for three days. There was no indigestion with this attack. Later there was some soreness over the region of the appendix. The bowels were loose whenever she was nervous.

It seems probable that the attacks of abdominal pain with vomiting and diarrhea were due to a smouldering tuberculous infection in the mesenteric lymph nodes. The synovitis in the ankles may well have been due to the absorption of toxins from the abdominal focus.

Case 5.—A college student, aged nineteen years, was seen first during August, 1924, complaining of pain and swelling in a number of joints. As a child she had had some severe illness with fever lasting two weeks. A playmate who apparently took the same infection died of it. She was well until January, 1924, when she had a pain in the right lower quadrant severe enough to keep her in bed for three days. There was no indigestion with it. A little soreness remained. Except for this she was well until April, 1924, when the left knee suddenly became swollen. A month later other joints became involved, one after the other. The tonsils had been well removed at the age of ten years.

Examination showed a well-built girl. The temperature was 37.6° C. There was a little swelling of the left knee and ankle. The right hand could not be closed. The heart was normal. The region of the appendix was tender. Roentgenograms showed calcified nodes to the right of the navel.

As tenderness about the appendix persisted and as the usual treatment for arthritis had little effect, operation was performed in September, 1924. The appendix was adherent to the cecum

and had apparently been inflamed. The spleen was twice normal size. There was one dense adhesion, probably congenital, running from the duodenum to the cystic duct. There was a large lymph node on the common bile duct, but the gallbladder appeared to be normal and all the nodes in the mesentery were enlarged. The appendix was removed and for a few months the patient improved; she had less trouble with the arthritis and regained much of her former strength. Later the joints again gave much trouble and improvement was slow. In June, 1925, the abdominal tenderness had gone and she was better. Digestion was good and she was able to walk without limping. In January, 1930, she reported that the tendency to arthritis was still present but her general health had remained good.

In this case, I believe, the focus of infection is in the mesenteric nodes where it has been smouldering, perhaps ever since the infection in childhood.

Case 6.—A woman, aged thirty-five years, was seen in January, 1925, complaining of sudden attacks of diarrhea. Her mother's father and mother had died of tuberculosis and the patient had been heavily exposed to the disease in childhood. When she was two years of age she nearly died with some form of dysentery. She was born and brought up in China. During her girlhood she occasionally felt a dull ache in the region of the appendix, and she was always annoyed by flatulence. In the summer of 1923 she suffered for a few days with nausea, vomiting, and diarrhea. In November, 1923, she was taken suddenly ill with knife-like pains in the abdomen, nausea, hematemesis, and melena. Amebiasis was found, treated, and cured. A few months later she had a severe cold and probably bronchopneumonia. She went to the country and there gained 26 pounds. She was well until November, 1924, when again there came a sudden attack of diarrhea, nausea, much soreness, and some pain in the region of the appendix, much flatus, and some heartburn. The abdomen remained sore for three weeks during which time there was one loose stool each morning. Amebae were looked for but not found.

A retrocecal appendix was then removed. On exploration of the abdomen nothing else was found to explain the symptoms. A few days after this operation the patient suffered another attack of nausea and diarrhea. In spite of dietary restrictions more attacks followed in close succession and the patient became extremely nervous. With the attacks there was a peculiar numbness in the arms.

Examination showed a well-built, fairly well-nourished woman, high strung, but sensible, cheery, and optimistic. The tongue was badly coated; the pulse was a little fast; the temperature was 37.2° C. The abdomen was not unusually tender. Sigmoidoscopic examination showed a normal rectal mucosa. Roentgenograms showed a normal stomach and colon, and a normally functioning gallbladder. To the left of the spine there were shadows of large calcified nodes. Gastric analysis showed normal amounts of total acid, but no free acid.

The giving of hydrochloric acid and albumin tannate (tannalbin) temporarily stopped the diarrhea, and the patient was sent to the country for rest, overfeeding, and heliotherapy. There she gained weight and strength, but she continued from time to time to have sudden attacks of nausea, diarrhea, crops of pimples, and a trembling feeling such as is experienced by one who has received an injection of epinephrine. In the attacks the pulse became rapid, and sometimes she felt a strange mental exhilaration as if she were going to be maniacal. These attacks came suddenly out of a clear sky, often when the patient was feeling well and happy; sometimes they woke her out of sound sleep. With some of them there was a little fever. Before the attacks she sometimes noticed the rumbling of rush waves down the bowel. In the next five months she gained 18 pounds; the attacks gradually decreased in frequency, and finally they disappeared. For the last four years she has been perfectly well.

Although I cannot be sure what the disease was in this case I suspect that there was a flare-up of low-grade infection, probably tuberculous, in lymph nodes that had been severely injured in childhood. A number of the symptoms suggested that the attacks were brought on by the sudden discharge of some secre-

tion or poison into the blood. Possibly the suprarenal bodies were involved in the disease.

Case 7.—A woman, aged thirty years, was seen in February, 1930, complaining of sciatica. At the age of fifteen years the

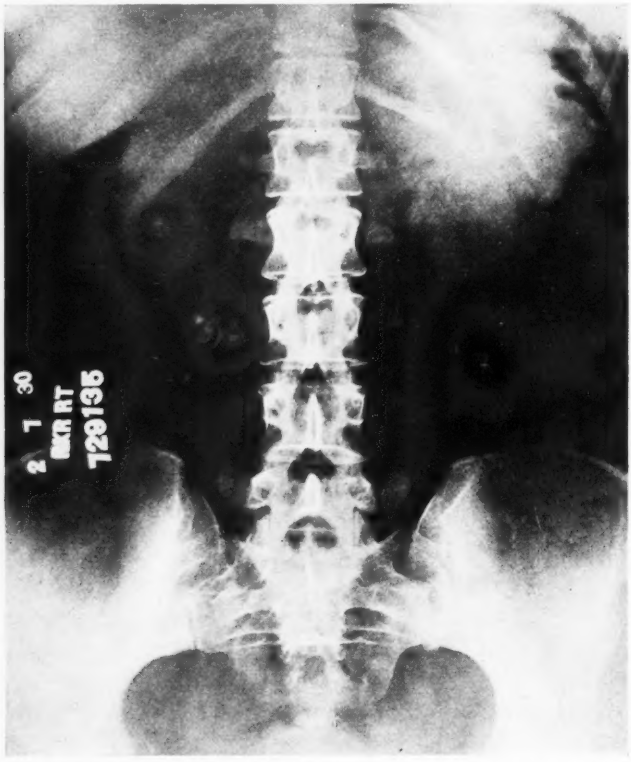

Fig. 132.—Calcified nodes in the right side of the abdomen due probably to severe appendicitis in youth.

patient was in bed for a month with a severe illness diagnosed at the time as appendicitis. There was no operation. Ever since then there had been times, especially when she walked fast,

when she felt pain in the lower right quadrant of the abdomen. In December, 1928, she had an attack of what appeared to be influenza and was in bed for three or four weeks. This was followed by suppurative inflammation in the ears and in the nasal sinuses and by severe sciatica. Ever since then the right sacroiliac region has been sore to the touch and there have been slight flare-ups of the pain in the leg. Roentgenograms showed calcified mesenteric nodes to the right of the spine.

It seems probable that these calcified nodes are relics of the old appendicitis and the question is whether they represent a focus of infection in the abdomen. None could be found elsewhere. It seems to me most likely that the infection which caused the recent inflammation about the spine entered by way of the respiratory tract and is now resident in the tissues about the spine. If there has been a flare-up of infection in the mesenteric nodes it is questionable how much influence appendectomy would have on it.

Case 8.—A farmer, aged forty-eight years, was seen in April, 1927, complaining of hematemesis. For ten years he had suffered with periodic attacks of indigestion which lasted several weeks and recurred at intervals of from one week to six months. The trouble consisted at first of a "pouring feeling" in the stomach and a dull "heaviness" relieved by soda or by the taking of food. There was no pain. Three years before coming to the clinic he vomited a large quantity of blood, and the stools were tarry for a week afterward. Similar bleeding took place about eight months before he came and also about two months before he came.

Examination showed an undernourished, pale, anemic man with foul teeth and a kyphotic spine. Repeated roentgen-ray examinations of the stomach showed nothing abnormal. The diagnosis was made of bleeding ulcer and after two transfusions the abdomen was explored. An ulcer could not be found. The first and second portions of the duodenum were dilated to twice the normal diameter and the wall was somewhat thickened, but there was no sign of obstruction at the duodenojejunal angle.

There was an area of hepatitis around the gallbladder but this organ appeared to be normal. The lymph nodes in the mesentery, particularly of the ileocecal part of the bowel, were markedly enlarged. The appendix was removed and the pathologist found signs of chronic inflammation in it.

The man improved markedly and gained 26 pounds in weight. In December, 1927, he wrote that any exertion caused him to bleed from the bowel; he did not say whether the blood was black or red. In December, 1928, he wrote that he was in better health than he had been for years.

One wonders if in this case the hemorrhage was due to chronic appendicitis or if the infection in the mesenteric nodes was primary and responsible for all the symptoms.

CONCLUSION

That mesenteric lymphadenitis can result fatally was shown in the case of a woman seen by me years ago. Unfortunately I cannot find the record so I cannot give details, but I remember that the main symptom was uncontrollable and unexplainable diarrhea. The woman failed and died, and at necropsy the only abnormality found was a remarkable hypertrophy of all the lymph nodes of the mesentery. There were scores of them, all discrete and about 2 cm. in diameter. Unfortunately the study of sections and cultures did not throw light on the underlying cause.

The question arises: Might not the disease in some of these cases be a mild form of Hodgkin's sarcoma? I think not. In the first place the patients rarely die as one would expect them to do if they had this serious disease, and in the second place, in my small experience the picture in the abdomen is very different with Hodgkin's disease from what it is with the lymphadenitis of unknown origin. With Hodgkin's disease some of the nodes become very large and many of them fuse into still larger masses. I have yet to see this take place in the cases of lymphadenitis; there the nodes remain discrete.

It seems to me probable from the cases that I have seen that the most common cause or forerunner of the disease is juvenile tuberculosis. Lewis has suggested that in some cases the infect-

ing organism may be *Brucella abortus* and this possibility will have to be kept in mind by future students of the disease.

Ever since I read years ago the stimulating papers by Adami on subinfection (on the stream of bacteria which is constantly passing from the bowel down the mesentery and into the lymph nodes at its root) it has seemed to me probable that many of the strange disorders of digestion that are associated with slight fever, nausea, bloating, abdominal soreness, signs of reverse peristalsis, diarrhea, inanition, and arthritis could best be explained on the basis of such low-grade infection. In some cases the appearance of crops of pimples in the skin, together with slight fever, flare-ups of inflammation in the joints, and feelings of malaise and weakness have convinced me that organisms of low virulence were getting into the blood stream.

One of the greatest needs of medicine today is for some means of raising the resistance of the body to such infections. In many cases I believe we could get results if we could treat the patient exactly as we would treat him if we knew that the infection was a tuberculous one. Unfortunately we physicians can rarely do this because we are not sure that prolonged rest, overfeeding, and heliotherapy will effect a cure; we are hesitant in our advice and the patient drifts on trying first one medicine and then another. I think it is worth noting that in a number of the cases just described the patient recovered only after long-continued treatment of the type that is used in sanatoriums for the tuberculous.

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IRRADIATION AS A MEANS OF DIFFERENTIATING CERTAIN VARIETIES OF TUMORS

ARTHUR U. DESJARDINS

NUMEROUS and extensive experiments on animals and abundant clinical evidence have established the fact that every variety of cell in the body and every organ or structure composed largely of one variety of cell has a specific sensitiveness to roentgen and radium rays. The investigations of Heineke, Thies, Warthin, Krause and Ziegler, Rudberg, Aubertin and Bordet, Arella, Regaud and Crémieu, Pappenheim and Plesch, Lazarus-Barlow, Tsuzuki, Piepenborn and many others have conclusively shown that the lymphocytes in the spleen, lymph nodes, intestinal lymph follicles, bone marrow, circulating blood, and thymus gland are the most sensitive cells in the body. Warthin, for example, found that within fifteen minutes after exposing the entire body of animals to roentgen rays, the lymphocytes in the spleen and other lymphoid structures began to disintegrate and that such destruction progressed for several days. The effect was perceptible first in the nucleus, the chromatin of which became fragmented and scattered between the remaining intact cells. After about three days the fragmented chromatin was taken up by reticular cells which assumed phagocytic properties and swelled as the amount of ingested chromatin increased. This was followed by gradual intracellular digestion of the chromatin débris. Such destruction of lymphocytes, which was partial or practically complete, according to the dose of radiation, was accompanied by temporary arrest of mitotic division of the intact cells and by marked diminution in size of the irradiated lymphoid elements; this continued for some time, but later, when the dose of rays had been small or moderate, a variable degree of regeneration of the lymphocytes occurred. The cellular changes

described by all other investigators have been essentially the same.

The organs next to the lymphoid tissues in sensitiveness to radiation are the testis and ovary. Such sensitiveness of the genital glands does not apply to all the cells, but only to the basal epithelium of the seminal tubules and ovarian follicles. The susceptibility of the testis to irradiation is due to the special sensitiveness of the spermatogonial cells; the cells of Sertoli are comparatively resistant, and the spermatocytes and spermatozoa are affected only secondarily, as the injured or destroyed spermatogonia fail to mature. In the ovary the corpus luteum and interstitial tissue are relatively resistant to the action of the rays. The influence of radiation on the basal epithelium of the seminal tubule and ovarian follicle is such that part or all of these cells fail to mature, and hence the function of the glands can be arrested temporarily or permanently, according to the dose of rays to which the structures are exposed.

All other cells in the body likewise have a specific radiosensitiveness, by which is meant that each variety of cell reacts to a given dose of roentgen or radium rays in a characteristic manner and at a characteristic rate. Moreover, the susceptibility of normal and pathologic cells of the same kind is essentially the same; cells forming part of a disease process tend to be more sensitive than normal cells, but the difference is seldom great enough to make a distinct clinical impression. Factors other than the specific sensitiveness of cells, it is true, may play a more or less important part in the reaction of pathologic tissues to irradiation. Among such factors are the degree of malignancy of a tumor, and the abundance of its blood supply, but all these factors combined have less influence on the reaction of cells to roentgen or radium rays than the natural irritability inherent in the cells themselves.

Knowledge of the specific sensitiveness of different cells often enables the expert radiologist to distinguish certain tumors by the rate and degree of regression after exposure to the rays. Indeed, in connection with some tumors such as those included under the generic term of lymphoblastoma and embryonal

carcinoma of the testis, such differentiation is proving itself almost as accurate as microscopic examination, which is now too generally held as infallible. This claim may seem exaggerated until attention is called to one or two important points. Usually the pathologist must base his opinion of the character of a tumor on the microscopic appearance of one or several small sections of tissue from one or more parts of the growth. And yet it is well known that different parts of many neoplasms vary much in architecture and cellular morphology. When a tumor is irradiated, on the other hand, the entire growth is exposed to the influence of the rays, and homogeneous tumors made up largely of one kind of cell retrogress at a specific rate and in a specific manner. Moreover, the rate and manner of regression of a tumor agree closely with the known radiosensitiveness of its normal cellular prototypes. It must be admitted that different tumors of the same kind often exhibit variations in reaction, but only occasionally is the range of such variation sufficient to cause serious confusion.

To those who are unfamiliar with the influence of radiation on normal tissue this doctrine of the specific sensitiveness of cells may appear revolutionary, but its validity with reference to the more sensitive kinds of cells can be demonstrated at any time. Pathologists need not be disturbed, however, because the differential value of irradiation applies only to certain varieties of tumor, and because such differentiation requires several days to several weeks. Even this small delay, in many cases, would not meet the requirements of the surgeon, who often must know at once the essential character of the tumor, but when such delay is not crucial, when a biopsy is not advisable, or when the patient refuses to submit to the procedure, it may still be possible to distinguish certain neoplasms and to do the patient good at the same time.

Microscopic examination by a competent pathologist is justly recognized as the most accurate means of identifying the character of tumors, but even the best pathologist is not infallible. Indeed, the greater his ability, the more willing he is to modify or reverse his opinion. Surgeons and clinicians generally

are too prone to accept a pathologic report without reservation, regardless of important and conflicting clinical circumstances. If the ability of the pathologist accurately to identify the character of tumors cannot be rated as 100 per cent, the acumen of the surgeon in this respect must be still lower, and on the average must vary as the difference between the microscope and the unaided vision. The most experienced surgeons are often surprised to find that a tumor which, at the operation, had the appearance of a carcinoma later proved to be quite a different tumor. The literature of medicine is crammed with reports based on an erroneous designation of tumors, and this probably accounts for some of the current legends about the eccentric behavior of malignant growths.

TUMORS ARISING IN LYMPHOID STRUCTURES

The neoplasms most readily identifiable by the characteristic and exceptional sensitiveness of the lymphocytes of which they are largely composed are those which develop in the lymphatic or lymphoid structures generally. The reaction of such tumors is usually so great and corresponds so closely to that of normal lymphocytes that irradiation constitutes a valuable therapeutic test and enables the recognition of such tumors aside from any difference in their clinical features. A few examples to show the rapidity with which lymphoid tumors are influenced by irradiation may not be amiss. Figure 133 illustrates the appearance of a patient when first seen, August 6, 1929. The tremendous enlargement of the cervical and axillary nodes is only too obvious. Figure 134 shows the same patient after fifteen days of treatment with roentgen rays. During this short interval, the size of the nodes had diminished 50 per cent, and the enlarged nodes continued to retrogress for some time afterward. Such rapidity of recession is a certain indication of a malignant condition derived from lymphoid tissue. Only lymphoid cells can react to irradiation at this rate. Lymphosarcomatous tumors sometimes react even more rapidly than those associated with Hodgkin's disease or lymphatic leukemia, but in the average case the difference is hardly sufficient to serve as a sharply distinctive feature. But

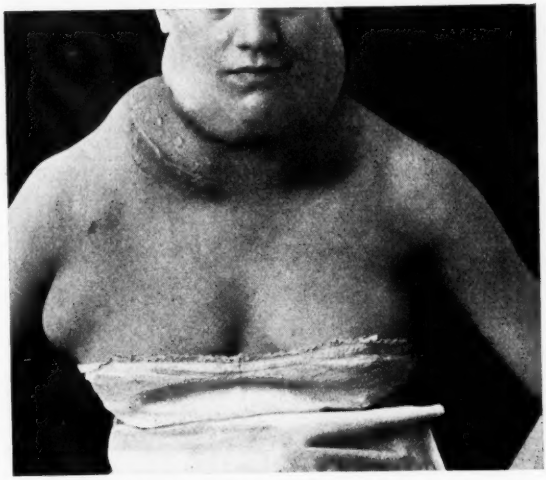

Fig. 133.—Patient August 10, 1929 before treatment.

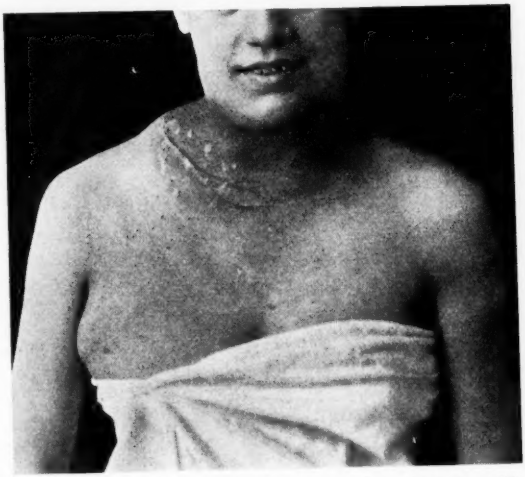

Fig. 134.—Patient shown in Figure 133, August 27, 1929 after fifteen days of roentgen ray treatment.

although, in the majority of cases, the reaction to irradiation cannot differentiate clearly the different varieties of lymphoblastoma, it is almost always sufficiently characteristic to distinguish any variety of lymphoblastoma from any other kind of tumor.

Figures 135 and 136 represent another example of the remarkable sensitiveness of lymphocytes and of tumors derived

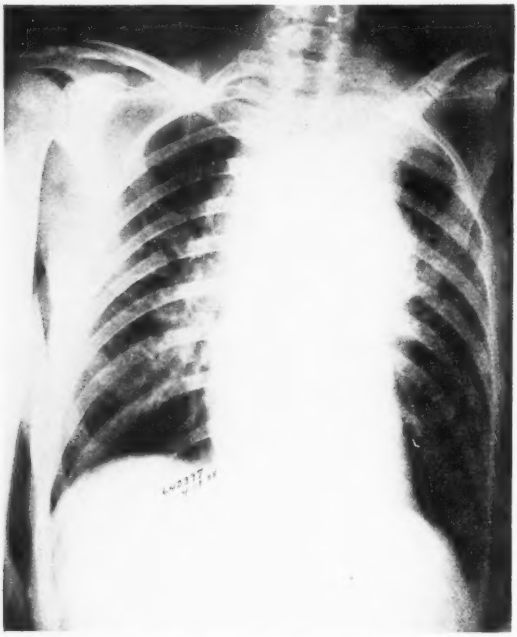

Fig. 135.—Roentgenogram, taken April 18, 1929, shows a large mediastinal tumor before treatment. Enlarged supraclavicular, axillary and inguinal lymph nodes were present also.

from them. Such a degree of regression within three or four weeks after exposure to roentgen rays cannot mean anything else than a lymphoid tumor. This is shown even more clearly by Figures 137 and 138. Such rapid decrease in the size of a tumor is observed only in lymphoid growths. An epithelioma,

carcinoma, and all other varieties of tumor, except those originating in lymphoid organs or structures and composed chiefly of lymphocytes, react more slowly when they react at all.

Regaud, Reverchon and Covtard, Schmincke, and Jovin called attention to a group of tumors arising usually around the tonsil,

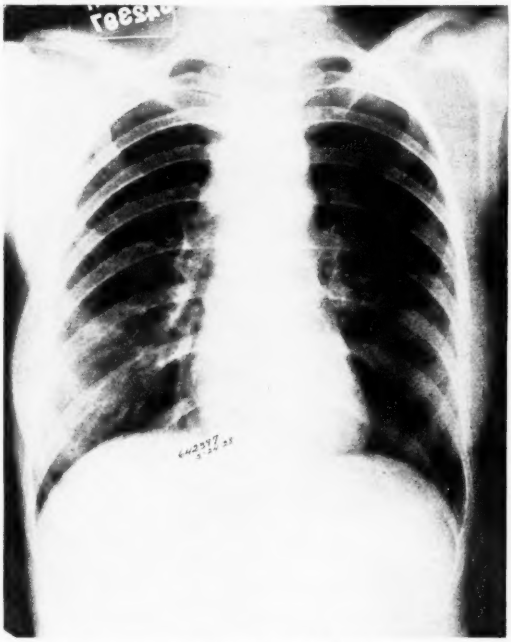

Fig. 136.—Roentgenogram taken May 24, 1928, shows marked reduction in size of mediastinal tumor following a single course of roentgen irradiation. The size of the superficial lymph nodes is smaller (same case as shown in Figure 135).

base of the tongue, or nasopharynx, the microscopic appearance of which so resembles epithelioma as to deceive the most competent pathologists, but which contain a considerable proportion of lymphoid cells, and the radiosensitiveness of which corresponds to that of lymphoid tumors in general. Often the patient is unaware of the primary growth, but the initiated laryn-

gologist is generally able to find it. In some instances, however, no trace of the primary tumor can be discovered in the nasopharynx. Regaud gave to such tumors the name of lymphoepithelioma. This interesting observation naturally led to the suspicion of a special relationship between the lymphoid and epithelial cells of such neoplasms. That this was no idle con-

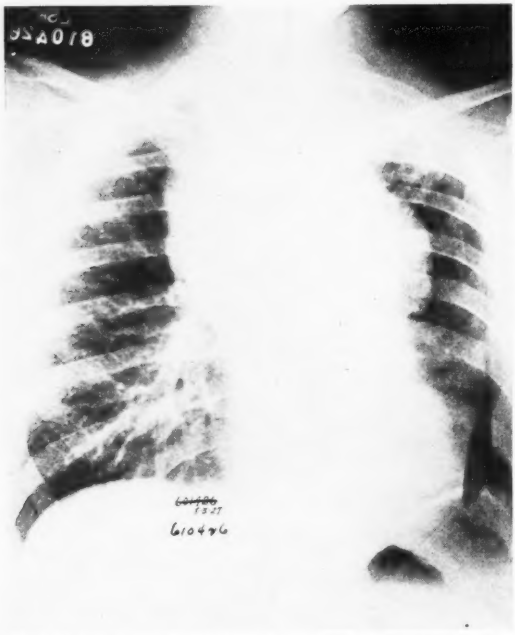

Fig. 137.—Roentgenogram taken August 3, 1927, shows a large mediastinal tumor before treatment. Enlarged supraclavicular and axillary lymph nodes were present also.

jecture may be surmised from the antecedent investigations of Jolly and Mollier, who tried to ascertain if some special relationship between lymphoid and epithelial tissue in certain parts of the body might not explain the apparently anomalous behavior of such tumors. They found that, in different species of animals, a special relation between the lymphoid and epithelial tissues

does exist in the nasopharynx, in the small intestine opposite the intestinal lymph follicles, and in certain other regions.

The following case is presented because it appears to be an example of lympho-epithelioma originating from the gastro-

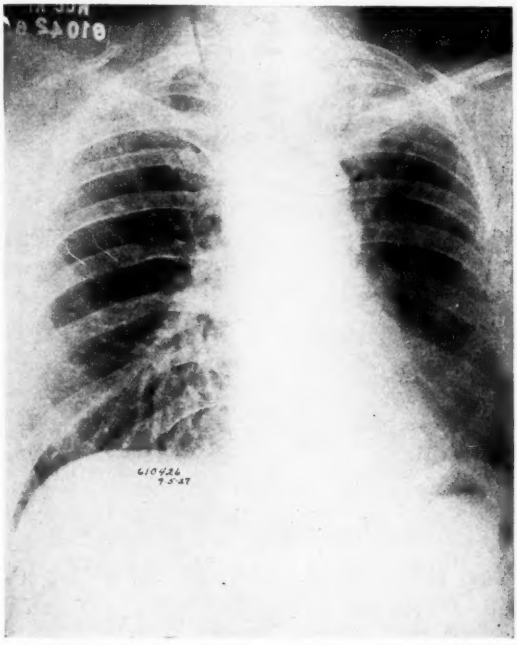

Fig. 138.—Roentgenogram taken September 5, 1927, shows marked reduction in size of the mediastinal tumor, and corresponding regression of the supraclavicular and axillary lymph nodes (same case as shown in Figure 137).

intestinal tract and because its recognition as a lympho-epithelial tumor was based mainly on its special reaction to roentgen irradiation.

Case 1.—A man, aged forty-one years, registered at the clinic May 17, 1927, complaining of pain in the lower right quadrant of the abdomen. He had undergone hemorrhoidectomy in May, 1924, and stated that some abdominal disturbance mani-

fested itself by pain which appeared shortly afterward. At first the pain, which radiated to the right side of the scrotum, was not constant, but could be brought on by pressure or by tightening the belt. A general examination elicited tenderness around the right iliac fossa and a mass in the left upper quadrant of the abdomen. A roentgenologic examination of the gastrointestinal tract and a pyelographic examination of the urinary tract proved negative. An exploratory laparotomy was advised, but the patient decided to wait until later. When he returned to the clinic, January 30, 1928, the mass in the left upper quadrant of the abdomen had become more definite and had caused an aggravation of his symptoms. He was operated on, February 4, and the surgeon found a retroperitoneal tumor 7.5 cm. in diameter which appeared to occupy the middle and distal thirds of the pancreas. Several lymph nodes in the gastrocolic omentum were enlarged. The stomach, duodenum, and gallbladder appeared normal. The appendix was behind the cecum and was removed. At the same time, a specimen of the retroperitoneal tumor was taken, and the pathologist who examined it found carcinoma graded 4; the node from the omentum showed the same condition. Since it was impossible to remove the tumor, a drainage tube was inserted, and February 10 a tube containing 42 mg. of radium was introduced through the tube down to and in contact with the tumor, where it was left for six hours.

Between February 20 and 28, the patient was given a course of high-voltage roentgen irradiation through four large fields extending from the level of the xyphoid cartilage to a level 3 cm. below the umbilicus. The beam of rays directed to each of the two anterior and two posterior fields was made to converge toward the center of the tumor. The patient was then allowed to go home. When he returned to the clinic, April 11, he had gained 15 pounds in weight, his strength had correspondingly increased, and his general condition had improved considerably. The abdominal tumor could no longer be palpated. Nevertheless, between April 11 and 16, he received a second course of high-voltage roentgen irradiation similar to the first. After this his condition improved slowly, but steadily as far as

the abdomen was concerned, but shortly afterward he noticed that some of the lymph nodes in the neck were enlarging, and continued to enlarge until November, 1928, when he returned to have this feature investigated. Several enlarged nodes were found in the upper part of the neck on both sides, and November 17 and 19, 1928, the entire neck was exposed to roentgen rays of medium wavelength. The enlarged nodes gradually diminished in size and some of them disappeared during the next four weeks. Another course of roentgen-ray treatment to the neck was given, December 17. During the following month the patient's condition continued to improve and his weight increased 6 pounds, but he noticed slight tenderness adjoining the healed abdominal incision, so that the pressure of clothing was uncomfortable. When he was again examined, January 28, 1929, the lymph nodes in the neck were reduced to barely palpable fibrous granules, the abdominal tumor could not be palpated, and it was thought that the tenderness around the abdominal scar was probably due to the condition of the scar itself. The patient's condition remained satisfactory until September, 1929, when a small lump appeared in the submental region and grew rapidly. Aside from this, no evidence of tumor or adenopathy could be found. October 8, the submental nodule was irradiated and has been regressing steadily since that time.

This case is of unusual interest because of the pathologic diagnosis of carcinoma, graded 4 on the one hand, and because, on the other hand, the clinical features and the reaction to irradiation indicate a lymphoid rather than an epithelial tumor. It is certain that, if the abdominal neoplasm had been an ordinary carcinoma, it would not have responded to irradiation so rapidly or so completely, and that the patient undoubtedly would have been dead by this time. The foregoing facts lead one to consider the possibility or probability that the case here cited may represent a lympho-epithelioma arising from lymphoid structures in the retroperitoneal space, or perhaps related to the intestine. It is inconceivable that so malignant a tumor should have been not only arrested, but made to disappear or to remain quiescent for such a long time.

Many pathologists object to the term "lympho-epithelioma" on the embryologic ground that a lymphoid tumor cannot possibly arise from a tissue derived from the ectoderm, because the lymphoid structures are derived from the mesoderm. But such a contention overlooks an important consideration. While it is undoubtedly true that the lymphatic system in general descends from the mesoderm, it is no less true that certain essentially lymphoid structures, such as the thymus gland, are derived from the ectoderm. Indeed, the experimental evidence indicates that the reticular structure of the thymus gland descends from the ectoderm, while the lymphoid cells of the gland descend from the mesoderm, and this may serve to explain the epithelial appearance and the lymphoid radiosensitiveness of such tumors. Thus radiology bids fair to contribute an important link to the chain of pathologic knowledge and to add to our understanding of tumors as well as of purely physiologic processes.

TUMORS OF THE TESTIS

The only tumor which approaches lymphoblastoma in susceptibility to irradiation is the pure embryonal carcinoma, or seminoma, of the testis, but the clinical features of these two kinds of tumor are so well defined that confusion is seldom possible. The radiosensitiveness of the embryonal carcinoma of the testis corresponds closely to that of the normal spermatogonial cells which, as is well known, are the most sensitive cells in the testis, and which, next to the lymphocytes, are the most sensitive cells in the body. The reaction of the mixed, or teratoid, tumors of the testis is less rapid and less pronounced than that of the seminal carcinoma, and varies chiefly with the proportion of spermatogonial cells entering into their structure. Some of the mixed, or teratoid, tumors undergo a considerable degree of retrogression, but this is almost never complete or lasting. Few of the embryonal carcinomas retrogress completely, for that matter, but the degree of recession is greater, a certain percentage disappears completely, and this effect may last several years. In view of the embryologic and morphologic character of the mixed tumors, it is not surprising that they should be

affected less by irradiation. It appears fairly certain that total regression of a tumor of the testis and of its metastatic deposits indicates an embryonal carcinoma.

Case 2.—A man, aged thirty years registered at the clinic September 13, 1923. About a year previously he had begun to be distressed by abdominal discomfort, with pain, bloating, and belching from one to three hours after meals, and he had become aware of a mass about 3 by 5 cm. in the abdomen, to the left of and below the umbilicus. Two months later he was struck in the back by a motor car, after which he began to vomit one or two hours after meals and had severe pain in the back, but the vomitus was never tinged with blood. He also suffered from increasing constipation and lost 25 pounds in weight, in the course of about three weeks, but some of the lost weight was subsequently regained. The abdominal tumor gradually grew and became quite large. Early in August, 1923, an exploratory laparotomy had been performed elsewhere, and the patient was told he had a malignant condition of the stomach and that it could not be removed. General examination disclosed a smooth, firm ovoid tumor measuring about 10 by 15 cm. in the lower half of the abdomen, about two-thirds of the mass being to the left of the median line and the upper pole at the level of the umbilicus. The growth could be readily felt through the rectum as a large, solid, fixed and tender mass. A nodule 2 cm. in diameter was found in the left half of the scrotum. It was obvious that there was a tumor of the left undescended testis, with metastasis to the iliac and retroperitoneal nodes as well as to the pilot node in the left supraclavicular region.

Surgical measures being contraindicated, the patient was given, between September 17 and 22, 1923, a course of treatment with roentgen rays of medium wavelength directed to the entire trunk and to the supraclavicular region on both sides. When he returned to the clinic, November 26, his weight had increased 14 pounds, he had not vomited for thirty days, his bowels were regular, the pain had greatly diminished, the abdominopelvic tumor could no longer be palpated, and the en-

larged supraclavicular node was now represented by a few small granules. A second thorough course of roentgen irradiation was given between November 27 and December 3, 1923, after which his condition continued to improve, and he has remained well since, without further treatment.

Such complete and permanent regression of a metastatic tumor as large as 15 cm. probably means that it was a pure embryonal carcinoma. A mixed, or teratoid, tumor would almost certainly not have receded so rapidly or completely, and the patient would undoubtedly have succumbed in the meantime.

BENIGN GIANT-CELL TUMOR OF BONE

Another tumor, in which the reaction to irradiation is sufficiently characteristic to act as a valuable diagnostic sign, is the true benign giant-cell tumor of bone. I believe it was Herendeen who first clearly described the effect of radiation on this tumor, an effect which, so far as I am aware, is not observed in any other kind of growth. About ten days after exposure to a moderate dose of rays of medium wavelength the tumor begins to swell, and the swelling is accompanied by redness of the skin and increased pain. If not warned, the patient as well as the attending physician or surgeon is naturally led to deduce that irradiation has stimulated the tumor to increased growth and may be tempted to interfere. A limb may thus be unnecessarily amputated. After about two weeks the swelling, redness, and pain subside and disappear; new bone is gradually deposited in the tumor, and in the course of from six to twelve months the tumor may be replaced by solid and healthy bone. Unfortunately, the diagnosis of giant-cell tumor involves a grave responsibility, because some of these neoplasms contain malignant elements; if any uncertainty exists, the conscientious surgeon must remove, or give the patient the benefit of, the doubt. Economic factors also may have to be considered. Nevertheless, the knowledge of the specific reaction of pure giant-cell tumors to irradiation may save many limbs which otherwise would be ruthlessly sacrificed. One course of treatment is generally sufficient and a large quantitative dose is undesirable. Prolonged or

continued treatment induces repeated reactions which may lead to delay in repair of bone. Overtreatment, therefore, is to be avoided.

BONE TUMORS

Most malignant tumors of bone are only slightly or moderately susceptible to irradiation. Few such tumors are ever cured permanently by any method of treatment. Nevertheless, in this group also the reaction to roentgen or radium rays may sometimes help in establishing the diagnosis.

Case 3.—A man, aged thirty years, registered at the clinic October 1, 1925, complaining of "rheumatism." He had been well until nearly two years previously, when he noticed a slight pain in the lumbar portion of the back on the left side. The pain slowly increased in severity and three months later began to radiate to the left hip and down the left thigh as far as the knee, and caused the patient to limp. The pain, which was worse at night, often interfered with sleep, but walking, heat, and rubbing usually gave relief. Medication and the extraction of three teeth not bringing any improvement, a plaster over the lumbar region was found more helpful. Although the pain was thus relieved, the lameness gradually increased. Three weeks before registration the pain returned, varied in intensity, became progressively worse, and appeared to be independent of climatic changes. The patient had lost 20 pounds in weight, and had not been able to work for some time.

General examination disclosed slight weakness and atrophy of all the muscles of the left lower extremity, and severe pain on flexion of the left thigh. A roentgenographic examination of the lumbar spine and pelvis revealed a tumor involving and destroying much of the left ilium and suggesting a giant-cell tumor or an endothelial myeloma (Fig. 139). Surgical measures appearing out of the question, a course of irradiation through three large fields, with rays of short wavelength, was given October 8, 9, and 10, 1925. This was followed by rapid disappearance of pain and lameness, by increase in weight, and by corresponding improvement in general condition. A reaction suggestive of

giant-cell tumor did not occur. A second roentgenographic examination of the pelvic bones on the left side showed decided improvement in the condition of the ilium. A second course of irradiation with roentgen rays of short wavelength was given December 10, 11, and 12, 1925. The patient's condition continued to improve, and he remained virtually free from pain in the back

Fig. 139.—Roentgenogram taken October 2, 1925, shows a tumor causing extensive destruction of the left ilium.

and left hip, but he had during the previous five days occasional pain in the right thigh, along the distribution of the right sciatic nerve. February 25 and March 1 and 2, 1926, a third course of irradiation with rays of short wavelength was given, again through three fields, but the size of the anterior and posterior fields was increased so as to extend well beyond the median line and to include all the presacral and lower lumbar lymph nodes on the

right side. The pain disappeared almost completely during the next few months, and the patient's condition improved steadily. When he was again examined, between September 23 and 29, 1926, pronounced amelioration in the condition of the left ilium was shown by the roentgenograms (Fig. 140). He was allowed to return home without treatment.

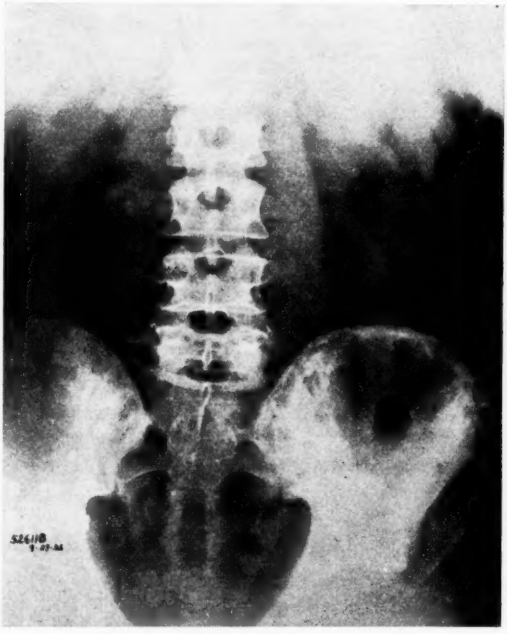

Fig. 140.—Roentgenogram September 27, 1926, shows marked regression of tumor and regenerative repair of the left ilium (same case as shown in Figure 139).

During the next six months the condition of the patient was excellent. Except for an occasional slight pricking sensation around the left knee and a "tired feeling" in th back, he was free from pain and able to do his usual work on he farm. He remained well until the beginning of May, 1927, when attacks of pain, similar to that from which he had suffered previously,

returned at intervals of three or four days, and the attacks gradually became more frequent. Roentgenographic examination of the pelvis, June 1, 1927, showed increased density of the left ilium and irregularity in the textural lines of the bone. This, together with the pain and a slight depression in the general condition of the patient, indicated recent malignant activity. For this reason a fourth course of irradiation through six fields with roentgen rays of medium and short wavelengths, was given between June 1 and 10, 1927. This was followed by rapid disappearance of all symptoms, and except for occasional slight soreness in the back and around the shoulders, the patient's condition has since been excellent.

In the absence of biopsy the character of the neoplasm is somewhat uncertain in that an absolute distinction cannot be made between benign giant-cell tumor and endothelial myeloma of Ewing. In view of the reaction of the growth to irradiation, a reaction entirely different from that which characterizes giant-cell tumors, it is almost certain that the tumor in this case was an endothelial myeloma.

COMMENT

The expert radiologist can render valuable assistance in the recognition of certain kinds of tumor, and such assistance is not confined to the varieties of neoplasm which have been described. If his knowledge of the radiosensitiveness of normal and pathologic tissues enables him to identify certain tumors with a considerable degree of accuracy, such tumors also can be excluded by this means; this may narrow the diagnosis sufficiently in some cases to bring other neoplasms within the scope of the radiotherapeutic test.

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TYPHOID VACCINE IN THE TREATMENT OF NEUROSYPHILIS

PAUL A. O'LEARY

IN several previous communications I have called attention to the value of nonspecific measures in the treatment of neurosyphilis. The first report was made in 1925, and the subsequent annual observations have substantiated Wagner von Jauregg's original report. At first, treatment by malaria was used only in cases of general paralysis, but continued observation and experience led to its use not only in these cases, but in cases of asymptomatic neurosyphilis, in cases in which the condition of the spinal fluid had not been reversed by the routine specific measures, and in cases of serologically negative tabes dorsalis with persistent pains in the legs and gastric crises. My results in the treatment of patients with uncomplicated tabes dorsalis have not been as successful as in the treatment of patients with general paralysis in 38 per cent of whom an economic remission has been maintained at the end of four years.

Treatment by malaria requires institutional care, by a staff specially trained in the care of such patients. The difficulty of obtaining the *Plasmodium vivax* in certain parts of this country probably will not warrant the general use of the method. Kunde, Hall, and Gerty recommended the use of typhoid vaccine in place of the *Plasmodium vivax* as a means of producing a course of fever. The facilities offered by typhoid vaccine over treatment by malaria are obvious. Typhoid vaccine not only offers a controllable course of fever, but it also may be used to provoke chills and fever in patients who have aborted the malaria. I have used it also in cases in which the malaria has been aborted after the fifth or sixth chill and in which reinoculation with *Plasmodium vivax* has failed. In such instances six or ten in-

jections of typhoid vaccine have been given to complete the pyrexial course.

Because of the difficulties and complications met with in treatment by malaria, a variety of substances and systems have been recommended, among them rat bite fever (Sodoka), relapsing fever, hot-water baths, diathermy, and vaccines of various sorts. Although sufficient time has not elapsed to make definite appraisal of these methods, it is possible to gather impressions of those that have been tried and observed for two years or more. I shall report the results of observations of a group of forty-eight patients with neurosyphilis of various types, who were given from one to four courses of typhoid vaccine.

Twenty intravenous injections of the typhoid vaccine constituted a course. The injections were given every other day, and the courses were repeated at intervals of five to seven months. It was the practice to give 25,000,000 bacilli intravenously at the first injection, and to increase the subsequent injections gradually, with the purpose of producing the maximal reaction within the bonds of safety. Certain individuals acquire a resistance to the vaccine so that it becomes impossible to produce a febrile reaction. In my experience with treatment by malaria, the outstanding therapeutic results were observed in the patients who ran the most intensive course of fever, that is, those who had an average temperature of 104.5° F. or more, and a series of approximately twelve fever bouts. An endeavor was made to simulate this type of course with the typhoid vaccine.

The complications encountered in treatment by typhoid vaccine are less numerous and less severe than in treatment by malaria. Mild toxic dermatitis of the erythematous type, jaundice, slight anemia, loss of weight, and arthralgia were among the most frequently noted complications. In the tabetic patient the exaggeration of lightning and girdle pains, and occasionally urinary retention, were the most troublesome symptoms dealt with during the course of fever. The exaggeration of the lightning pains was the outstanding complication noted; this frequently necessitated the liberal administration of morphine

following each injection. I shall report here three cases which illustrate the result of treatment by typhoid vaccine.

Case 1.—A man, aged twenty-six years, acquired syphilis in 1918, and received an indeterminate amount of treatment at the time.

When the patient came under my care in November, 1926, the Wassermann reaction of the blood and of the spinal fluid was strongly positive; the Nonne reaction was positive; there were 22 lymphocytes for each cubic millimeter in the spinal fluid, and a zone II or tabetic type of colloidal benzoin curve. The neurologic examination was negative for signs of parenchymatous neurosyphilis, although the patient's family had noted a change in personality, forgetfulness, and loss of ambition. A diagnosis of neurosyphilis was made, possibly of the paresis sine paresi type.

Between November, 1926, and June, 1927, the patient received two courses of combined intravenous and intraspinal injections, in conjunction with forty-six intramuscular injections of succinimide of mercury and large doses of iodides. At the end of this time the spinal fluid was still strongly positive, and treatment by malaria was recommended. He gave a history of having had malaria in 1920. He was inoculated with two different strains of the *Plasmodium vivax* a week apart, but they failed to "take." The injection of foreign protein and of whole blood did not precipitate the chills and fever. Following a course of quinine, typhoid vaccine was given intravenously. Fifteen injections were given at intervals of two days. The initial injection contained 25,000,000 bacilli, and the dose of each subsequent injection was increased until 400,000,000 bacilli were given at each of the last three treatments. On the day of the last injection the patient noticed icterus. Within three days he was markedly jaundiced, and the test of hepatic function showed the extreme degree of dye retention, serum bilirubin of 22.4 mg. and a direct van den Bergh reaction. The blood smears were still negative for *Plasmodium vivax*. Duodenal lavage was carried out, mild cathartics were given, and a diagnosis of mild toxic

hepatitis was made. In less than three weeks the jaundice had disappeared. Two months later the tests of hepatic function were negative, and the patient had gained 8 pounds. It was suggested that he should not receive treatment for the next nine months. On his return at the end of this time he had gained 20 pounds; he had lost many of his "neurotic complaints," and had carried on his work during the previous nine months. There was no change of significance in either the blood or spinal fluid. Practically the same status was noted when he returned a year later.

Case 2.—A woman, aged thirty years, the mother of one healthy child, came to the clinic in October, 1926, because of

TABULATION

TREATMENT AND SEROLOGIC CHANGES IN CASE 2

Date course of treatment was started.	Arsphenamine, gm.	Mercury succinimide, grains.	Sodium iodide, gm., intravenously.	Intraspinal treatment.	Mercury inunctions.	Spinal fluid.			
						Wassermann reaction.	Nonne reaction.	Lymphocytes for each cubic millimeter.	Colloidal benzoin curve, zone.
10/ 9/26	1.9	3.5	200	3	..	++++	Positive	203	I
2/10/27	..	..	....	..	30				
4/ 5/27	2.4	3.0	....	3	..	++—	Positive	4	II
6/10/27	..	..	....	..	24				
10/13/27	1.8	3.6	....	3	..	++—	Positive	6	II
11/15/27	..	..	....	..	40				
2/29/28	1.7	3.3	....	3	..	2—	Negative	4	II
6/10/28	..	..	....	..	40				
10/ 6/28*	..	..	....	..	..	3—	Negative	1	II
4/ 4/29†	..	..	....	..	..	Negative	Negative	2	II
11/12/29†	..	..	....	..	..	Negative	Negative	3	II

* Sixteen intravenous injections of typhoid vaccine.
† No treatment.

backache. During the course of the examination a strongly positive Wassermann reaction of the blood was noted. Examination of the spinal fluid revealed a strongly positive Wassermann reaction (44444), positive Nonne reaction, and 190 small lymphocytes, 11 large lymphocytes, and 2 polymorphonuclear leukocytes in each cubic millimeter. The colloidal benzoin curve was reported as zone 1 or the paretic type. There were no clinical signs of syphilis or clinical evidence of neurosyphilis. The treatment was rather intensive and is summarized, together with the changes in spinal fluid, in the tabulation on page 642.

Case 3.—A boy, aged eight years, with congenital syphilis which had been recognized and treated rather indifferently, came to the clinic in July, 1928, because of increasing difficulty in walking, and more recently difficult articulation.

Neurologic examination disclosed parenchymatous neurosyphilis, and it was felt that cerebral palsy and mental deficiency was combined with the neurosyphilis. The Wassermann reaction of the blood and of the spinal fluid was reported as strongly positive, and the Nonne test was positive; there were 10 cells for each cubic millimeter of spinal fluid, and a zone I (paretic) colloidal benzoin curve.

The child was inoculated with *Plasmodium vivax*, July 16, and eight days later the first chill developed. He had two subsequent chills and courses of fever following which the malaria aborted spontaneously. Efforts to revive the chills and fever were futile, so a course of intravenous typhoid vaccine was inaugurated. The first injection consisted of 5,000,000 bacilli, and the eighth injection, the last of the course, consisted of 150,000,000. Treatment was not given during the next six months. At the end of this time his mother was extremely enthusiastic about the result. The child had gained 8 pounds, was decidedly brighter, walked more easily, and also talked more distinctly. The Wassermann reaction of the spinal fluid was then negative, and the Nonne reaction was positive; there were 4 cells in the spinal fluid and a zone II colloidal benzoin curve. The Wassermann reaction of the blood was still positive.

Because of the child's general improvement, another course of typhoid vaccine was given. The first injection consisted of 5,000,000 bacilli; at the sixteenth injection, the last in the series, 300,000,000 bacilli were injected. Six months later he returned, still further improved in his manner, walking, talking, interest, and mental capacity. The Wassermann reaction of the blood remained positive, although the reactions of the spinal fluid had reversed to negative in all respects.

These three cases are the outstanding examples of the results from typhoid vaccine in a series of forty-eight cases in which the treatment was given and the patients were observed for at least eighteen months.

Observation of the results of treatment by typhoid vaccine in neurosyphilis has not substantiated the early impressions from its use, and fall far below those from malaria or tryparsamide. I have not had sufficient experience with other methods to make comparative deductions. There have been no economic remissions produced in the paretic group that are comparable to those observed following treatment by malaria, and the serologic changes have not been significant. In the nonparetic group, the results have not been encouraging. As many as four courses (more than sixty injections) have been given in a few of the cases in which the reaction of the spinal fluid has been persistently positive, but the serologic changes have been slight.

I still use typhoid vaccine as an adjuvant to treatment by malaria when the patient spontaneously aborts the malaria before having completed the prescribed number of chills with fever, and also as a means of reactivation if abortion of the malaria is threatened.

THE RELATIONSHIP OF THE EMOTIONS AND CUTANEOUS LESIONS

WILLIAM H. GOECKERMAN

IT is still a common attitude of the profession to assume that a patient is ill-balanced mentally if it is suggested that the medical problem he presents may be the result of his emotional life. In the light of careful clinical observation and such facts as have been established by laboratory and clinical research, a somewhat more critical attitude should teach us that this is not necessarily true. Nor is it implied that such a patient has an obscure mental complex which must be expurgated by a freudian type of psychoanalysis or some other type of psycho-analysis. In fact, it seems to me that tangible organic changes must occasionally result from emotional disturbances if our knowledge of the autonomic nervous system and its physiology is correct. Given the proper predisposing and precipitating conditions, a normal person, no matter how well balanced mentally, need not be considered exempt from such changes. It is true that in the presence of a sensitive mentality, a mercurial disposition, and a tense dynamic personality, such changes are more likely to develop than in the presence of equanimity. It should be recalled also that an individual's emotional life is not necessarily written on his features so that any one who runs may read. He need not be the so-called "nervous" type of individual. The ordinary emotions such as anger, fear, worry, and ambition when dominating mental life for a considerable period are probably sufficient to produce gross anatomic changes. I wish to emphasize this statement by citing briefly a few dermatologic cases, which I think bring corroborative clinical evidence, and I feel certain that any physician who has interested himself in the emotional

life of his patients, will recall similar instances, if not of disturbances of the skin, then of some other organ.

About two years ago, I examined a farmer, aged sixty years, with typical lichen planus. His actions were those of a man of this type; he was quiet, reserved, and seemingly stolid. On direct questioning he denied any worry or anxiety except that connected with the routine of a rural existence. He was given the conventional treatment by roentgen ray, arsenic, and mercury, with various local applications, without material benefit, for a considerable period of time. Repeated interviews with reference to a possible emotional factor had been unproductive. The itching was intense. He had written to his oldest son about his difficulty. The son lived at a considerable distance, and his father had not seen him for many years. The son visited the old home and later called at the clinic to get an opinion on his father's disease. After a brief explanation of lichen planus, the possibility of emotional factors and worry was mentioned. The son said at once that his father had feared for a number of years that he might lose his farm. The patient had not mentioned his worry to any of his other children. He had told his oldest son during the recent visit that there was still a mortgage of $2,000 on the farm, that it had not been possible for him to reduce this sum, and that there had been years when he had met the interest only with great difficulty. Realizing that his efficiency was decreasing with his advancing years, he saw nothing but foreclosure ahead. Fortunately for the patient, the son was in a financial position to adjust matters. The mortgage was paid, and the farm rented, with the son's knowledge of all the details. The patient retired to a small town. The itching subsided promptly and the lichen planus involuted rapidly without further medication.

About six months ago a woman, aged forty-five years, came to the clinic with dysidrotic eczema of the hands. As new vesicles appeared, they sometimes reached the size of large bullae with considerable inflammatory reaction, a picture answering very well to the description of cheiropompholyx in the text-books. General examination did not reveal anything of significance, and

it seemed as though symptomatic treatment would have to be relied on, although the patient had consulted a number of physicians who had at one time or another used various conventional measures, without benefit. Her second visit at the clinic was the result of her husband's illness rather than her own. He had been sick for nearly two years and treatment had not benefited him, nor had she ever, to her own satisfaction, been told the nature of his trouble. While the husband was undergoing general examination she was under my observation because of dysidrosis. Although the wife was outwardly well poised, it was nevertheless suspected that the worry over her husband's illness was probably responsible for the dysidrosis. When I learned from her that her husband had hyperthyroidism, which she was told could probably be relieved by an operation, I somewhat facetiously ventured the opinion that her skin trouble would probably disappear if her husband's operation proved a success. The operation was a success and my prognosis was verified.

I have mentioned lichen planus and dysidrosis as manifestations of the skin resulting from emotional disturbance. This list can readily be augmented and examples cited of other manifestations, for example, urticaria, pruritus ani, pruritus vulvae, and other types of localized pruritus, dermatitis herpetiformis, eczema, and probably other lesions that need not be mentioned here. This does not imply that such lesions of the skin are always the result of emotional disturbances, because there are other causes. It should be remembered that such manifestations of the skin are symptoms of an internal disturbance, slight or profound, and not disease entities. I do not wish to create the impression that the exact mechanism productive of the various lesions of the skin has been explained. I merely wish to emphasize the significance of emotional disturbances in the production of certain of the manifestations of the skin. As evidence that this assumption is not as heterodox as it may at first appear, let me call attention to Cannon's work showing increase of sugar and epinephrine in the blood, complete inhibition of gastrointestinal motility, and secreting activity, increase in the number of erythrocytes, and increase of blood pressure under emotional

stress. Grafe and Mayer found that the metabolic rate could be profoundly altered in certain persons by the suggestion of various calamities, for example, the death of a relative or the amputation of a limb. It has long been a well-known fact that emotional disturbances may affect menstruation, perspiration, and secretion of milk and urine; in fact, perhaps every visceral function is subject to influences exerted by emotional states.

All of these functional disturbances furnish abundant proof that the emotions must have a definite effect on the physiology of the body and hence on its chemistry. If such disturbances are repeated frequently, it is conceivable that in time they should leave a permanent imprint on the tissues of the body. It is an accepted fact that the emotions transmit their somatic and visceral impulses by way of the autonomic nervous system. The close functional relationship of this system with the endocrine organs will permit the visualization of organic changes in tissue as the result of emotional impulses. The significance of the emotions as factors in producing disease conditions is further emphasized by the fact that they have many of the characteristics of reflexes and are, therefore, not entirely under conscious control. More than that, in persons with unstable emotional balance, the emotions may become conditioned by indifferent stimuli. In such persons, the most trivial circumstances may be the constantly repeated source of emotional disturbances. In them, the emotions constantly upset the physiologic function of the body. I am convinced that the results of such disturbances can be as well if not better observed on the skin than on any other organ of the body. If this reasoning is correct or, at any rate, if the significance of emotional reactions in the production of certain lesions of the skin is admitted, then it is not logical to treat the signs and symptoms of emotional disturbances and ignore the fundamental factor. To be sure, it is not always easy, and sometimes it is impossible, to remove the cause of the emotional upsets. I believe, however, that the cases presented here will illustrate what can be accomplished when the emotions are given their proper place in the etiologic consideration of certain eruptions of the skin.

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SYSTEMIC BLASTOMYCOSIS

HAMILTON MONTGOMERY

I WISH to report a case of systemic blastomycosis and to distinguish sharply this disease in its systemic form, not only from coccidioidal granuloma and torulosis, but from various other conditions which may simulate it.

The term "blastomycosis" has been loosely used in the literature recently to cover the whole group of infections of the skin with yeast-like organisms. This has resulted in confusion. The term "blastomycosis," as used by dermatologists in this country, has been confined to the disease entity first described by Gilchrist in 1894. The causative organism, the blastomycete, has been variously named and classified by different mycologists.[1] It appears in human tissues as a refractile, double-contour, yeast-like organism which reproduces by budding. Mycelial filaments are not formed. In cultures it presents certain characteristics, including the formation of mycelium. Cutaneous blastomycosis presents as a rule a characteristic picture. The lesions simulate those of the verrucous type of tuberculosis of the skin, but with an elevated border containing many minute abscesses. The blastomycetes are usually readily demonstrable under the microscope in pus obtained from one of these abscesses and to which a drop of 10 to 30 per cent potassium hydroxide solution has been added. The clinical, etiologic, and pathologic features of the disease are fully considered and illustrated by Montgomery[6] and also in Ormsby's text-book.

Busse, in 1894, and Curtis, in 1896, have been given the credit for reporting the first and second cases of blastomycosis showing systemic involvement. As the result of recent investigation,[1, 3] however, it is doubtful whether either case can be cited as a true example of blastomycosis, the organism in Busse's case belong-

ing apparently to the cryptococci, whereas Curtis' case and perhaps even Busse's belong to infections from the true yeasts (Saccharomyces). The first undoubted case of systemic blastomycosis was that reported by Walker and Montgomery in 1902.[7] The systemic form of the disease may be divided into two groups: Dissemination of the disease to other parts of the body from a primary cutaneous focus, and a systemic onset involving one or more of the internal organs in the body. The earliest manifestations of this second type in the skin are the appearance of subcutaneous nodules which enlarge, become abscesses, and break through the epidermis. Through auto-inoculation of the skin from these abscesses, the characteristic verrucous lesions of cutaneous blastomycosis may eventually develop. The disease may affect any organ in the body. When the lungs are affected, the cases have often been confused with pulmonary tuberculosis. Exceptionally, however, both diseases may be found in the same individual.[7, 13] A comprehensive review of cases of systemic blastomycosis is given by Montgomery and Ormsby, Stober, and more recently by Michelson. The case which I am reporting belongs to the second type of systemic blastomycosis.

REPORT OF A CASE

A man, aged thirty-three years, came to The Mayo Clinic, June 14, 1926, because of generalized multiple cutaneous abscesses, together with destructive ulcerative lesions of both ankles. He was born in Wisconsin, of Canadian-American parentage. He was employed as a cook in a lumber camp in Wisconsin at the time his trouble started. The patient had been well until the middle of February, 1926, when he first noticed a slight nodular swelling on the right side of the thorax. This became larger, and finally broke through the skin and drained a large quantity of pus. It refused to heal. Similar lesions, all starting as subcutaneous nodules or abscesses, appeared on the face, hip, and arms. He first consulted a physician, March 22, 1926, because his ankles were tender and swollen. He could not give a history of cough or cold preceding the development of the abscesses. He had, however, noticed for several months an increased ten-

dency to sweat. When the patient was first seen by his home physician he presented multiple abscesses in the skin, some of which, on lancing, contained about 100 c.c. of pus. In a letter, his physician stated that the abscesses developed slowly; at first they were hard nodules and later they became soft. At no time did they show any inflammation. None showed a tendency to heal. Sloughing of the tissues and ankles had set in recently. Stock vaccine and autogenous vaccine had been used without benefit. Shortly before the patient came to the clinic, verrucous lesions developed about the chin and right cheek. He had lost 50 pounds in weight.

On admission the patient was slightly emaciated, and he was confined to a wheel chair because of destructive lesions of both

Fig. 141.—Systemic blastomycosis. Subcutaneous swelling on forearm may be noted.

ankles. On the thorax, abdomen, right thigh, and arms, were scattered isolated draining sinuses with a serosanguineous, purulent discharge (Fig. 141). Painless, subcutaneous nodules were palpable in both arms and on the abdomen. Figure 142 shows the verrucous character of the lesions on the face. The legs were relatively free, except the ankles (Fig. 143). The patient was hospitalized for further observation.

During the next nine days in the hospital general examination was essentially negative. Roentgenograms of the thorax were negative. Roentgenograms of both ankles showed marked destruction of the lower end of the tibia and fibula, probably the result of osteomyelitis. Roentgenograms of the palate showed rarefaction of the right side, extending through to the labial surface, involving teeth number 9, 10, and 11. Studies of the blood

Fig. 142.—Systemic blastomycosis. Abscesses on the thorax and the verrucous character of the lesions on the face are shown.

revealed mild secondary anemia; hemoglobin was 60 per cent, erythrocytes numbered 3,600,000, and leukocytes 12,000. Examination of the urine, including an anlysis for bromides, was negative. Examinations of the stools for parasites and ova were negative. The Wassermann reaction of the blood was negative. Several cultures made from pus obtained from an abscess were

reported negative for ordinary bacteria, and up to the ninth day for blastomycetes. A smear of the pus showed a Gram-negative bacillus, but no acid-fast organisms. Biopsy of one of the subcutaneous abscesses was reported as inflammatory; however, the pathologist was not informed regarding the nature of the lesion and was not requested to search for blastomycetes.

Fig. 143.—Systemic blastomycosis. Part of the ulcerations are the result of surgical manipulation.

The diagnosis of blastomycosis was first established June 23, when typical double-contour budding organisms were demonstrated in potassium hydroxide preparations of pus obtained from a minute abscess from a lesion on the chin and from a similar lesion on the thumb. Aspiration of a beginning abscess on the abdomen also revealed many typical blastomycetes. Cultures were reported positive July 7. Because of a suggestion of

endosporulation, the laboratory report favored a diagnosis of *Coccidioides immitis* (the organism of coccidioidal granuloma). Further studies were, therefore, made of potassium hydroxide preparations of the pus from various abscesses. They all showed typical blastomycetes reproducing by budding and in no in-

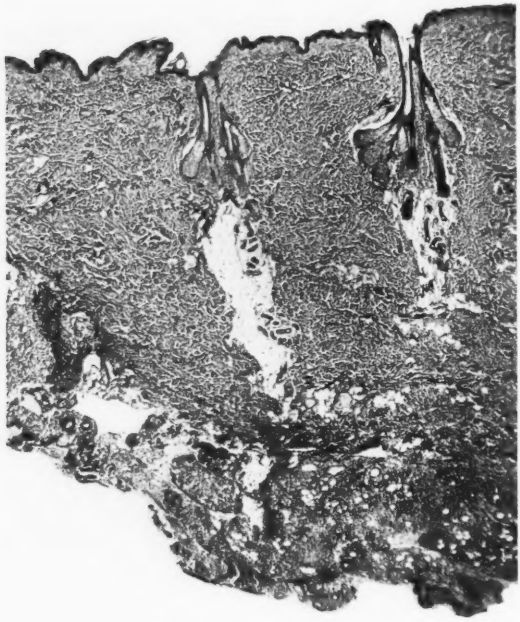

Fig. 144.—Systemic blastomycosis. The skin epidermis and cutis are free from any changes. The extent of formation of abscess deep in the subcutaneous tissues may be noted (× 18).

stance by endosporulation. A review of the biopsy also showed typical budding organisms in the sections.

The histopathologic picture of the subcutaneous abscess is shown in Figures 144, 145, and 146. The epidermis and cutis did not show pathologic changes. In the subcutaneous tissue, however, there was a large diffuse abscess containing serum,

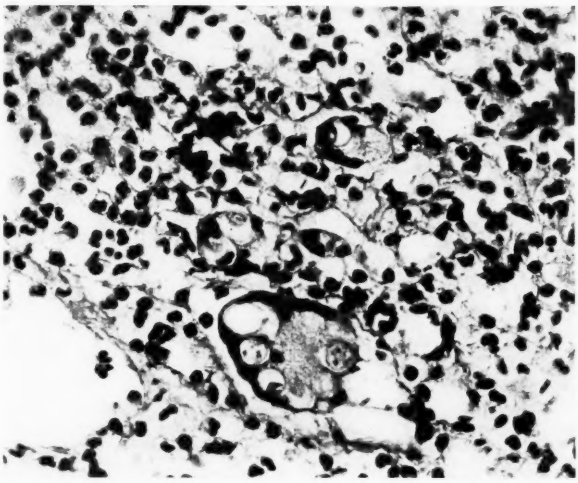

Fig. 145.—Systemic blastomycosis. Center of abscess. Numerous refractile double-contour organisms may be noted (× 350).

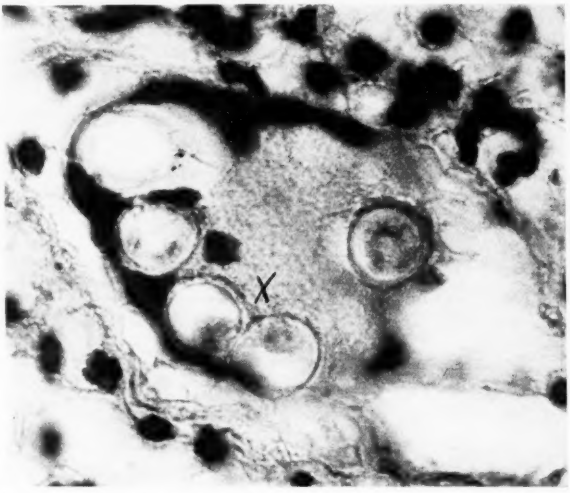

Fig. 146.—Systemic blastomycosis. Character of the blastomycetes in a giant cell, also terminal stage of budding at × are shown (× 900).

polymorphonuclear leukocytes, lymphocytes, plasma cells, and giant cells of the Langhans type. Very few epithelioid cells were present. There was no tubercle formation. In localized areas in the abscessed region, there were numerous refractile double-contour organisms, both within the giant cells and lying free in the spaces of the tissues. Many budding forms were demonstrated. In no instance was endosporulation seen. None of the organisms showed a zoöglea-like membrane or capsule.

The patient remained in the hospital for four months, during which time his temperature fluctuated from 99° to 101.5° F., occasionally rising to 103° F. The temperature curve was septic in type with a daily afternoon rise, together with a corresponding rise in pulse. As soon as the diagnosis was established, the patient was started on increasing doses of potassium iodide by mouth and sodium iodide intravenously up to a total of 600 grains a day. There was marked improvement; the abscesses dried up in part and the temperature dropped to a maximum of 100° F. In August, however, the iodides began to lose their beneficial effect and were stopped. Two injections of neoarsphenamine were given and the patient became worse. Roentgen rays were applied locally to the lesions and by systemic deep therapy. Iodides were again resumed by mouth and were increased to the patient's tolerance of 960 grains a day. Local treatment consisted in the use of potassium permanganate wet dressings, and later a 1 per cent solution of copper sulphate. New lesions continued to appear, including several in the scalp. September 5, the patient had a convulsive seizure which was followed by several other attacks. Bilateral bronchopneumonia developed a day before death. Death occurred October 13, eight months after the onset of the disease. Shortly before death, a roentgenogram of the thorax was negative except for elevation of the diaphragm on the right to the level of the fourth rib. Repeated blood cultures for blastomycetes were negative.

Postmortem examination revealed blastomycosis of the ankles with multiple subcutaneous abscesses and ulcers, ulcer of the scalp, and calvarium with chronic local pachymeningitis, a nodule in the left testis, fatty changes and hypertrophy of the

liver, old healed pulmonary tuberculosis, and bilateral bronchopneumonia. Microscopic studies confirmed the foregoing data. Blastomycetes were demonstrated in the meninges in large numbers, including many budding forms. There was no evidence of formation of a capsule or of a zoöglea-like membrane. Blastomycetes could only be demonstrated in two of five sections of skin taken from the edges of the ulcer. Bone from the leg or calvarium was not removed for microscopic study. A careful search for blastomycetes in sections from various parts of the lung and other organs failed to reveal their presence.

This case is one of systemic blastomycosis involving the skin, meninges of the brain, and probably also the bones of the leg and calvarium. The case is unusual in that the lungs are involved sooner or later in most instances. The failure of various laboratory methods to establish the diagnosis in the beginning shows the necessity at times of repeated careful search for the blastomycetes with all the methods at our disposal. Search for the blastomycetes either in potassium hydroxide preparations or in sections must be made with a minimal amount of light entering the microscope. The demonstration of the organisms in only two of five sections of skin removed at necropsy may be explained on the basis of poor selection of the areas for biopsy. It is possible also that the large doses of potassium iodide may have reduced the number of blastomycetes. Marked progression of the lesions on the ankles followed surgical incision done early in the course of the disease. It has been my experience that in cutaneous blastomycosis, there is danger of dissemination of the disease through attempts at excision, curettage, or similar procedures. Practically all cases of systemic blastomycosis have a fatal termination in spite of any treatment that may be given.

Coccidioidal granuloma, in spite of the literature to the contrary, may be indistinguishable clinically from certain cases of blastomycosis. The case reported showed involvement of bone and dry verrucous lesions on the face similar to those in Chipman and Templeton's second case. Clinically, however, in cases of coccidioidal granuloma there is usually marked involvement

of the lymph nodes, whereas this is not common in cases of blastomycosis, as dissemination usually occurs through the blood stream. The two diseases may be definitely differentiated by the fact that *Coccidioides immitis*, the cause of coccidioidal granuloma, always reproduces in tissues by endosporulation and never by budding, whereas the blastomycete in tissue always reproduces by budding.

Torulosis[12] is a disease caused by a yeast-like organism which attacks primarily the brain and meninges. McGehee and Michelson, however, recently pointed out that there are two groups, one the systemic type with fatal termination, and the other a local type ending in recovery. Rappaport and Kaplan reported a case of torulosis showing involvement of the skin as an acneform lesion, as well as infection of the blood stream and spinal fluid. The organism causing the disease is about the same size as the blastomycete and reproduces by budding. It differs, however, from the blastomycete in tissues in that it has a distinct capsule or zoöglea-like membrane, and in cultures there are certain differences, such as the failure to form mycelium. The distinction made for both torulosis and coccidioidal granuloma, that in sections there is no minute abscess formation, is only relative. I have seen cases of blastomycosis which at some stage of the disease presented the histopathologic picture of granuloma without the formation of abscesses and in which the blastomycete was demonstrated.

That blastomycosis, torulosis, and coccidioidal granuloma are closely related, there can be no doubt. Systemic disease due to infection by true yeasts might also be considered in this group. Histoplasmosis of Darling is another rare systemic disease due either to a protozoan or to a yeast-like organism which so far as I know has not been reported as causing lesions on the skin. Mycologists do not appear as yet to agree entirely in their classification of the different organisms. I believe these diseases should be carefully distinguished from one another on the basis of present knowledge.

Unusual forms of scrofuloderma of the skin may at times be confused with systemic blastomycosis. I recently saw a patient

who presented multiple abscesses and sinuses, together with pulmonary symptoms. The histopathologic picture suggested a diagnosis of scrofuloderma. Blastomycetes were not present in smears, in cultures or in sections of tissue. Definite acid-fast bacilli showing all the morphologic features of bacilli of tuberculosis were finally demonstrated in the sections.

Extensive pyoderma of the skin, iododerma, bromoderma, and glanders are usually readily distinguished from cases of systemic blastomycosis by their concomitant clinical data and history, and by bacterial, chemical, and pathologic studies.

The systemic type of blastomycosis arising from a primary focus in the skin may be simulated by sporotrichosis or by tularemia of the ulcerogranular type. In both of the latter diseases, spread of the infection by the lymphatics is an outstanding feature. This, with the history, and cultural and other laboratory data, permit definite differentiation.

SUMMARY

A case of systemic blastomycosis is reported which presented, at first, certain difficulties in diagnosis. The distinction of blastomycosis from coccidioidal granuloma, torulosis, and various other conditions is considered.

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ATYPICAL PULMONARY SEPSIS SIMULATING SEPTICEMIA: REPORT OF A CASE

E. LeRoy Kellum and Norman M. Keith

This case is presented to show the marked similarity of clinical symptoms between intrapulmonary infection and general septicemia. It also illustrates the difficulties of clinical diagnosis in many cases of sepsis.

A woman, aged twenty-eight years, was admitted to the clinic December 24, 1929, and was sent immediately to the hospital for medical care. She had always been subject to colds, and associated with such colds had had a protracted cough which was productive of mucus. Except for these colds, which she herself minimized, she was entirely well prior to the birth of her first child, November 15, 1929. She apparently had had a normal pregnancy with no untoward symptoms. After a thirty-hour labor she was delivered of a normal male child by forceps under chloroform anesthesia. Twenty-four hours after delivery she had a subnormal temperature with chilliness, headaches, restlessness, muscular pains, and syncope. Forty-eight hours after delivery, she had a very severe and prolonged chill followed by a sudden rise in temperature to 105° F. with profuse perspiration and extreme weakness. Following this, for five weeks previous to admission, she had had from one to three severe chills daily, followed by a sudden rise of temperature up to 105° F. with profuse perspiration and weakness. She had lost 20 pounds, and was so weak that she could not raise her head from the pillow. Her local physician had noted progressive anemia. At no time had there been pelvic pain, or foul lochia, or bloody or foul discharge from the pelvis. Repeated pelvic examinations had been made without disclosing evidence of pelvic infection. Iron and quinine sulphate had been given by mouth.

The pulse was 140; the temperature was 103.5° F., and respirations 46. The systolic blood pressure was 140 and the diastolic 70. The patient was extremely pale, dyspnea was marked, and respirations were hurried and shallow. The skin was sweaty. The tongue and lips were dry and parched, and the patient seemed dehydrated and was very toxic. There was a constant dry, hacking cough which was not productive, and was not affected by change of position. The breath was not foul, and petechiae could not be seen on the skin, the conjunctiva, or the mucous membrane. Erythema, edema, jaundice, pain, and swelling in any of the joints were likewise absent. Examination of the nose and throat was essentially negative. The pupils were round and equal, and reacted to light and accommodation. Kernig's sign and stiff neck were absent, and the reflexes were equal and normal. Examination of the ocular fundi showed that the disks were somewhat anemic and retinitis of the toxic type was present. The pulse was accelerated but regular. The heart was not enlarged, the right border being 3.5 cm. and the left border 10 cm. from the midsternal line. A soft systolic murmur was heard at the mitral area, which was not transmitted to the axilla and disappeared when the patient was upright. The heart action was regular and the sounds were of good quality. Persistent nonconsonating medium and coarse bubbling râles were heard over the base of both lungs, chiefly at the right base. There was dulness to percussion over the left upper lobe and prolonged expiration over the right upper lobe. The abdomen was essentially normal. There was no tenderness, no rigidity, and no mass. The spleen was not palpable, nor was the edge of the liver. The cervix uteri was soft; bilateral lacerations were healed. The uterus was one and a half times normal size and there was no special tenderness or any definite masses or cellulitis. There was no discharge. Digital examination of the rectum was negative.

The hemoglobin was 23 per cent (Dare); erythrocytes numbered 1,900,000, and leukocytes 19,800, of which 88 per cent were polymorphonuclear neutrophils. The specific gravity of the urine was 1.014; it contained a trace of albumin, but no sugar, casts, erythrocytes, or pus cells. The blood urea was 20 mg. for

each 100 c.c.; the blood creatinine was 1.6 mg., the carbon dioxide combining power of the plasma was 58 volumes per cent, and the plasma chlorides were 584 mg. for each 100 c.c. Five daily examinations of sputum failed to reveal bacilli of tuberculosis. Several successive cultures of the blood made at the height of the chill failed to show any growth. Microscopic examination of catheterized urine also taken at the height of the chill was negative for pus and erythrocytes. The urine also failed to show growth by culture. The Widal test for typhoid was negative, as was the agglutination test for *Alcaligenes abortus*. A roentgenogram of the thorax disclosed pneumonia of the middle right lobe with apparently early abscess formation.

A clinical diagnosis of septicemia was made; the causative organism had not been determined. The condition of the lung was interpreted as intrapulmonary infection, with only one of the lungs affected in the general septicemia. It was believed that multiple small pulmonary abscesses were present without evidence of bronchial communication. Pulmonary infarction and bronchiectasis were also considered. Atypical tuberculosis, abscess of the liver, possible portal thrombosis and amyloid disease could not be ruled out. Because of the lack of symptoms at any time referable to the pelvis, such as pelvic pain or foul lochia, and because of negative pelvic examination, and the fact that the patient's illness started only twenty-four hours after delivery, a diagnosis of puerperal sepsis could not be made. In spite of the absence of embolic symptoms, such as petechiae, painful erythematous nodules, purpuric patches, pain in the joints, pain in the splenic area, palpable spleen, or jaundice, and the negative cardiac examination, bacterial endocarditis was considered.

The patient ran a typical septic, pyemic course with manifestation of infection of the blood. She had from one to three chills daily, repeated at irregular intervals, the rigor usually lasting from ten to thirty minutes. With each chill there was a sudden rise of temperature to 104° to 106° F. (Fig. 147), followed by marked sweating. It was necessary to change bedclothes

three or four times daily and once or twice at night. Marked prostration followed each chill.

The first eight cultures of blood, each taken at the height of the chill, failed to show growth at any time, although the cultures were preserved and examined at intervals for several weeks. Two cultures, taken later, however, were reported as showing an atypical streptococcus which grew under partial anaerobic conditions.

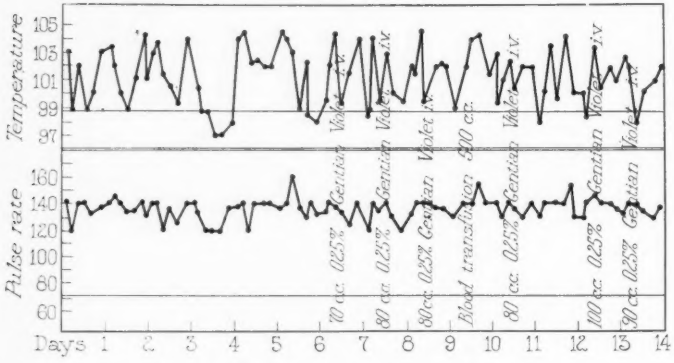


Fig. 147.—Section of temperature chart.

Repeated transfusions were given, after which the patient showed much clinical improvement. She gained in strength, appeared less toxic, and lost her pallor. After the fourth transfusion the hemoglobin had increased from 15 to 40 per cent, and the erythrocytes from 1,640,000 to 2,400,000. Sweating was also less marked, the appetite increased, and she took more food. She was given, in all, seven transfusions. Nine intravenous injections of gentian violet, averaging 80 c.c. of 0.25 per cent solution each were given. Mercurochrome was not given because the patient had been given this at home and had had a severe reaction from it.

For the first thirty days, the patient gained in strength and weight, and looked remarkably well, despite the repeated severe chills and fever. On the thirty-first day after admission, the patient appeared to be drowsy, and more toxic, and she vomited

repeatedly, the quantity measuring about 1,400 c.c. in a day. The following day the blood urea was 196 mg. for each 100 c.c. The plasma chlorides were decreased to 430 mg. for each 100 c.c. It is to be noted that the blood creatinine showed a normal reading of 1.8 mg. for each 100 c.c. One liter of 10 per cent glucose and 1 per cent sodium chloride solution was given intravenously on successive days. Following the second injection, the blood urea dropped to 63 mg. for each 100 c.c. Four days after starting the intravenous medication, the chemical and renal functional improvement was striking. The blood urea was 36 mg. for each 100 c.c.; the creatinine was 1.1 mg., and the plasma chlorides were 560 mg. The urinalysis during this period of dehydration and disturbance of renal function did not show change. The specific gravity varied from 1.010 to 1.015, with a trace of albumin and an occasional pus cell; casts and erythrocytes were absent. The urinary output was adequate. From this time until death the blood urea averaged 48 mg. for each 100 c.c. Dehydration is not uncommon after prolonged and marked loss of tissue fluids, particularly in high intestinal obstruction with repeated emesis. This patient had lost much fluid, both by emesis and excessive perspiration, following each chill.

Signs of consolidation in the left lower lobe of the lung, a gallop cardiac rhythm, and signs of myocardial failure eventually developed. The patient died forty days after admission.

Examination of the heart was negative repeatedly during the whole clinical course until the very last day, when signs of terminal cardiac failure appeared. The systolic murmur disappeared after transfusions of blood, and never reappeared, nor were other murmurs noted. The size of the heart was not increased, nor was there any aryhthmia.

At postmortem examination, the heart appeared to be normal; the endocardium and the valves appeared normal. Many miliary abscesses containing yellowish necrotic material were scattered throughout the caudal half of the upper left lobe of the lung. None of these abscesses measured more than 1.5 cm. in diameter. The lower left lobe contained three large bronchiec-

tatic abscesses, measuring approximately 2 cm. in diameter and filled with foul-smelling greenish-brown pus. One abscess was situated near the hilum, one at the base and one in the center of this lobe. There were, in addition, multiple miliary abscesses scattered through the lobe (Fig. 148). The cut surface of the upper and middle lobes of the right lung showed eight large bronchiectatic cavities (Fig. 149). The largest of these measured 5 by 2 by 3 cm., and the smallest measured 0.3 cm. in diameter.

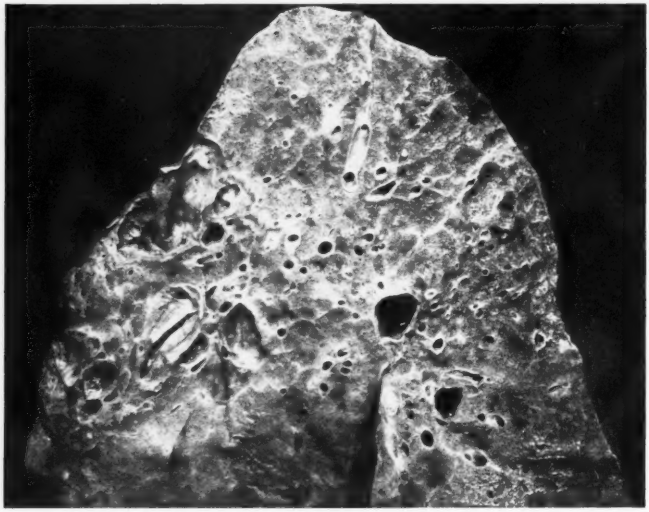


Fig. 148.—Bronchiectatic abscesses and several of the smaller abscesses.

There were numerous other similar cavities which were not revealed in the cut section. There were also numerous miliary abscesses whose diameter was approximately 1.5 cm. Abscesses were not seen in the cut surface of the entire lower lobe. Bronchopneumonia, involving the left lower lobe and the posterior inferior border of the lower right lobe, was rather widespread. The spleen weighed 400 gm. (normal weight 150 gm.) and showed moderate diffuse perisplenitis of the capsule. There were four splenic infarcts showing as a whitish, pink area in the capsule,

the largest of which measured 3.5 by 1.5 cm. The liver was hypertrophied and weighed 2,325 gm. (normal weight, 1,600 gm.). The esophagus, stomach, pancreas, right and left kidneys, both suprarenal glands, and the bladder all appeared to be normal.

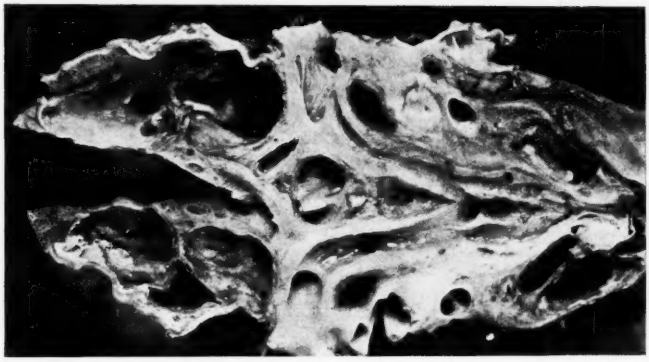


Fig. 149.—Cut section of the lung. Widespread and advanced bronchiectases are shown.

The vagina and cervix were normal. The uterus measured 8 by 5 by 3 cm. Both fallopian tubes and the ovaries appeared to be normal.

COMMENT

The case illustrates the possibility of the presence of widespread bronchiectasis with intrapulmonary infection without ready clinical diagnosis. It also illustrates that bronchiectasis may be symptomless rather than characterized by repeated persistent paroxysmal cough productive of foul-smelling sputum.

With clinical symptoms of general sepsis and with physical findings in the lungs, the possibility of diffuse intrapulmonary infection as the causative lesion must be carefully considered.

ELECTROCARDIOGRAPHIC LOCALIZATION OF MYOCARDIAL INFARCTS

ARLIE R. BARNES

As a result of a previous combined electrocardiographic and pathologic study of hearts in which coronary occlusion and infarction had taken place, Whitten and I concluded that there were characteristic modifications of the R-T and S-T components of the electrocardiogram by which one could predict whether the infarction involved the posterior basal portion of the left ventricle and the adjacent interventricular septum, on the one hand, or the anterior portion of the left ventricle, or the apex, or both, on the other. After localization of the area of infarction was made, it was possible to predict the artery involved provided the artery had its usual distribution. Furthermore, we concluded that when infarction occurred first in the region supplied by one coronary artery, and subsequently in the region supplied by the other coronary artery, and when they were separated by a sufficient interval of time, it was possible to predict the site of and the order in which the infarctions occurred if electrocardiograms were taken after each attack.

Certain modifications of the R-T or S-T segments of the electrocardiogram were found to be associated with infarction involving the anterior portion of the left ventricle and apex in the region usually supplied by the left coronary artery. The earliest electrocardiographic evidence consists of a change of level and contour of the S-T or R-T components in leads I and II and depression of the S-T component in lead III. The R-T interval in leads I and II, but especially in lead I, is elevated above the iso-electric line. The interval usually is convex, dome-shaped, or sloped downward toward the T wave. Diphasic T waves or T waves of a monophasic type are the rule in the earliest stages.

It is important to note that leads I and III act conversely, so that elevation of the R-T interval in lead I is opposed by depression of the S-T interval in lead III. The changes in lead II usually are similar to those in lead I in cases of infarction in the anterior portion of the left ventricle. At a later stage, the monophasic or diphasic type of T wave in lead I or in leads I and II is replaced by frank inversions. The T waves usually are deep, abrupt, or sharply peaked. It is noteworthy that as the T wave becomes inverted in lead I, the T wave in lead III remains upright, becoming exaggerated and sharply peaked. Of particular significance in this later stage is the rounded contour of the R-T interval in lead I or in leads I and II preceding inversion of the T wave. At this stage, the R-T segment approaches or reaches the iso-electric level (Table 1).

TABLE 1

SUMMARY OF THE ELECTROCARDIOGRAPHIC CHANGES OBSERVED IN INFARCTION OF THE ANTERIOR PORTION AND APEX OF THE LEFT VENTRICLE

Infarction of anterior portion and apex of left ventricle	1. Early stage 1–14 days after infarction	(*a*) Elevated R-T segment in lead I and usually in lead II. (*b*) Rounded convex or sloping R-T segment in lead I and usually in lead II. (*c*) Depressed R-T segment in lead III.
	2. Later stage 14 days to months after infarction	(*a*) Inverted T wave in lead I and usually in lead II. (*b*) Rounded or convex R-T segment in lead I and usually in lead II. (*c*) High, positive, sharply peaked T wave in lead III.
	3. Late stage 6–24 months after infarction	Gradual, partial and complete disappearance of the electrocardiographic changes in stages 1 and 2.

When infarction occurs in the posterior portion of the left ventricle, precisely the opposite set of conditions occurs. In this case, in the early stages, the R-T segment is elevated in lead III, and usually in lead II although to a smaller extent, and is depressed in lead I. The same convex, dome-shaped or sloping R-T segment preceding the T wave is apparent in leads II and III. In the later stages, the R-T segment in leads II and III tends to return to and eventually reaches the iso-electric level, and the depressed S-T segment in lead I disappears. In this stage

inversion of the T wave in leads II and III with a rounded contour of the preceding S-T segment is observed, whereas the T wave in lead I is upright and becomes exaggerated and more sharply peaked (Table 2). It must be emphasized that if the

TABLE 2

SUMMARY OF THE ELECTROCARDIOGRAPHIC CHANGES OBSERVED IN INFARCTION OF THE POSTERIOR BASAL PORTION OF THE LEFT VENTRICLE AND THE ADJACENT INTERVENTRICULAR SEPTUM

Infarction of posterior portion of left ventricle	1. Early stage 1–14 days after infarction	(*a*) Elevated R-T segment in lead III and usually in lead II. (*b*) Rounded, convex or sloping R-T segment in lead III and usually in lead II. (*c*) Depressed R-T segment in lead I.
	2. Later stage 14 days to months after infarction	(*a*) Inverted T wave in lead III and usually in lead II. (*b*) Rounded or convex R-T segment in lead III and usually in lead II. (*c*) High positive sharply peaked T wave in lead I.
	3. Late stage 6–24 months after infarction	Gradual, partial and complete disappearance of the electrocardiographic changes in stages 1 and 2.

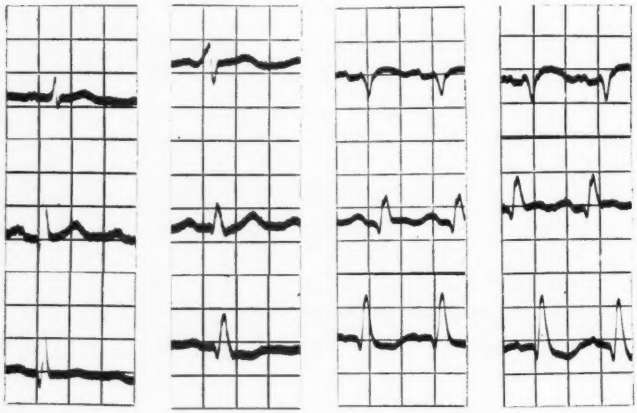
patient survives myocardial infarction of either the anterior or posterior portion of the left ventricle for a period varying from six months to two years, the evidence of inversion of the T wave tends completely to disappear and the electrocardiogram may not show abnormality.

Four cases are presented in which it was possible to predict the site of infarction by means of the electrocardiographic observations, and to confirm these predictions at necropsy.

REPORT OF CASES

Case 1.—A man aged fifty years came to the clinic for examination because of substernal pain. The complaint was first noted three months previous to examination, and followed an attack of influenza. The patient suffered from a dull gripping ache beneath the sternum in the third interspace which was brought on by exertion and eating, and was relieved by rest; the pain radiated down both arms. Dyspnea was an associated symptom.

On examination, the systolic blood pressure was 145 and the diastolic 80. The pulse rate was 116 and was regular. The apical heart tones were weak. The leukocyte count was 4,900. The electrocardiogram taken at this time did not show significant abnormalities (Fig. 150, *A*). Five days after this electrocardiogram was taken, the patient was seized with a severe gripping pain over the upper part of the lower half of the sternum, associated with marked weakness, pallor, profuse perspiration,



A *B* *C* *D*

Fig. 150.—Case 1. *A*, Electrocardiographic tracing taken five days before coronary occlusion; *B*, *C*, and *D*, tracings taken two, three and four days, respectively, after occlusion. The development of the elevated rounded S-T segment in lead I, the gradual elevation of the R-T segment in lead II, and the progressive formation of a depressed R-T segment in lead III are shown.

cold extremities, and dyspnea. The pain radiated into both arms and lasted for twelve hours, despite the fact that hypodermic injections of morphine were given. On examination, the patient had an ashen color, and the skin was moist and cool. The heart tones were distant and tic-tac in quality. The systolic blood pressure was 90, and the diastolic 72. The leukocyte count was 11,800; 87 per cent of the leukocytes were neutrophils. Leukocyte counts on successive days were 19,400, 15,000, and 14,800.

The temperature reached an elevation of 101° F. on the second and third days following the onset of the acute pain. Electrocardiograms taken the first, second, and third days after infarction showed an elevation of the S-T segment in lead I with an upward convexity, an elevation of the R-T segment in lead II, and a gradually increasing depression of the R-T segment in lead III (Fig. 150, *B*, *C*, and *D*). On the basis of these changes a

Fig. 151.—Case 1. *P*, Posterior portion of left ventricle; *I*, zone of infarction and thinning involving the apex, anterior portion of left ventricle and adjacent portion of interventricular septum; *T*, apical thrombus.

diagnosis was made of coronary occlusion with myocardial infarction which involved the anterior portion of the left ventricle or apex, or both, in the region usually supplied by the left coronary artery. Assuming that this region received its usual blood supply, it was predicted that the occlusion involved the anterior de-

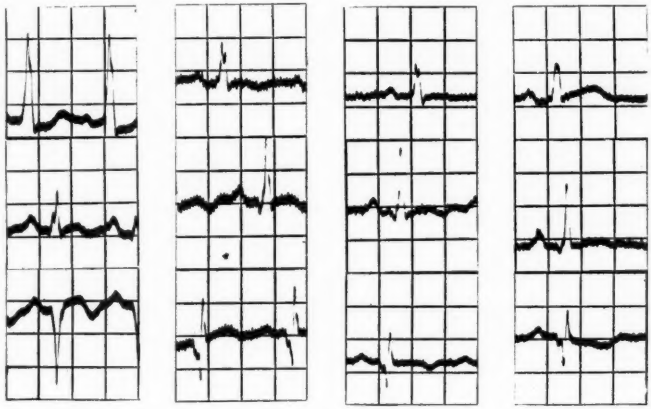
scending branch of the left coronary artery. Death occurred on the fourth day from cardiac failure.

At necropsy, the heart weighed 460 gm. A yellow fibrinous exudate covered the entire visceral pericardium and injection of the vessels of the pericardial surface was marked. The anterior surface of the left ventricle and the apex were diffusely stained and infiltrated with blood. The muscle was softened over the region of the apex, the anterior portion of the left ventricle, and the adjacent interventricular septum for a distance of 5 cm. from the apex. The ventricular muscle was thinned out over that area and the septum bulged into the right ventricle. Attached to the endocardium over this area of softening was a large mural thrombus (Fig. 151). Sclerosis, graded 2, was present in the right and left coronary arteries. The anterior descending branch of the left coronary artery was occluded 5 cm. from its orifice by a thrombus, and at that point the lumen of the vessel was nearly obliterated by arteriosclerosis. The aorta was only slightly sclerotic.

Case 2.—A woman, aged fifty-four years, February 5, 1929, was awakened in the night by an agonizing, crushing pain in the upper part of the epigastrium, radiating around the lower right costal margin and upward beneath the sternum. Her physician gave her two hypodermic injections of morphine which afforded only slight relief. The pain lasted for two days and the patient remained in bed for four days. There was great weakness associated with the attack. After that, and until admission to the hospital, exertion, especially when she faced a cold wind, produced substernal pain and dyspnea similar to that experienced in the original attack, although of less severity. The pain was always relieved by rest.

On examination the patient was found to be obese; the systolic blood pressure was 200 and the diastolic 120. The pulse rate was 120 and was regular. There were no noteworthy changes in the cardiac sounds, but the heart was moderately increased in size. Examination of the fundus oculi showed hypertension type of sclerosis, graded 3, of the retinal arteries. The leukocyte count

was 9,200. A roentgenogram of the gallbladder by means of the Graham-Cole technic did not show abnormality. The electrocardiogram, taken April 24, revealed depression of the R-T segment in lead I, a rounded positive convexity of the R-T segment in lead II followed at times by an inverted T wave and at other times by a diphasic T wave, and an elevated R-T segment in lead III with distinct positive convexity followed by inversion of the T wave (Fig. 152, *A*). On the basis of these observations,



A *B* *C* *D*

Fig. 152.—Case 2. *A*, Electrocardiographic tracing taken on admission and before second coronary occlusion. The depressed R-T segment in lead I and the rounded convex S-T segment preceding the negative T wave in lead III may be noted. *B*, *C*, and *D*, Tracings taken the second, third, and fifth days, respectively, after the second coronary occlusion. The gradual elevation of the R-T segment in lead I with the development of the rounded contour in lead I and the disappearance of the rounded convexity of the R-T segment in lead III with replacement by the depression of that interval in the last electrocardiogram may be noted.

and in conjunction with the history, a diagnosis was made of ancient infarction in the posterior basal portion of the left ventricle in the region usually supplied by the right coronary artery. It was assumed that the infarction corresponded with the attack of pain, February 5, which has been described.

The patient was admitted to hospital, April 30, complaining

of severe lower substernal pain of twelve hours' duration. This pain persisted for about thirty-six hours, but there was a residue of soreness across the upper part of the abdomen on the third day. The leukocyte count was 14,200 the second day after the onset of pain and 14,400 the following day. The blood pressure was 160 systolic and 110 diastolic the day of admission; 105 systolic and 70 diastolic the third day, and 102 systolic and 70 diastolic the fifth day following admission. Electrocardiograms taken the second, third, and fifth days following admission to the hospital showed a marked change in the R-T segments when compared with the tracing taken on examination at the clinic. The R-T segment in lead I was no longer depressed and had begun to take on a positive convexity. The R-T segment in lead III, on the contrary, had lost most of its elevation above the iso-electric line, and the depth of the T wave inversion was distinctly decreased. The R-T segment in lead II had lost most of its upward convexity and the T wave tended to become more nearly iso-electric (Fig. 152, *B*, *C*, and *D*). These changes in the electrocardiogram were contemporaneous with clinical events indicating acute myocardial infarction, and the changes observed were practically a neutralization of the changes noted with the assumed ancient infarction of the posterior surface of the left ventricle. The logical deduction was that these changes represented infarction in the anterior portion of the left ventricle or apex in the region usually supplied by the anterior descending branch of the left coronary artery. The patient died suddenly during the night of the seventh day in hospital.

At necropsy, the heart weighed 478 gm. Ancient infarction in the posterior and basal two-fifths of the left ventricle was present. By dissection, this region was shown to be supplied by branches of the right coronary artery. An area of acute infarction began 2 cm. posterior to and included the apex, and involved the anterior portion of the left ventricle and the adjacent septum to a distance of 6 cm. from the apex (Fig. 153). The dissection of the anterior descending branch of the left coronary artery showed that it supplied the area of acute infarction, including the posterior aspect of the apex. The right

and left coronary arteries were sclerosed, graded 3. The aorta was sclerotic, graded 2. The valves of the heart were normal.

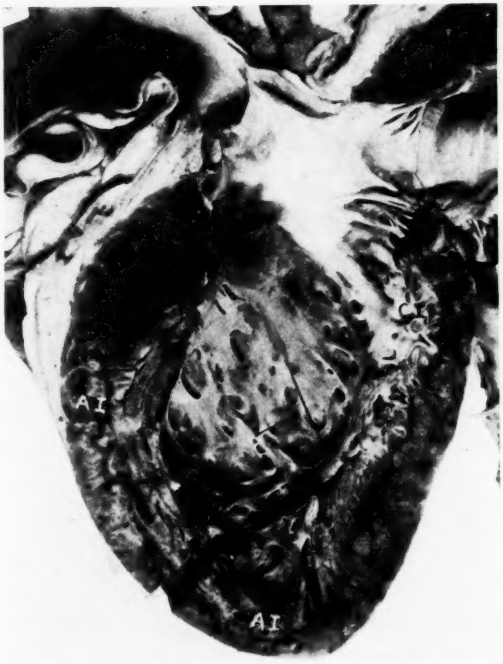


Fig. 153.—Case 2. *CI*, Chronic infarction involving the posterior basal portion of the left ventricle and the adjacent interventricular septum; *AI*, acute infarction involving the apex, the anterior portion of the left ventricle and the adjacent interventricular septum.

Case 3.—A man, aged fifty-two years, came to the clinic complaining of pain in the thorax and dyspnea. For three years, at infrequent intervals on exertion, he had experienced dyspnea and pain in the lower substernal area which were relieved by rest. One week prior to admission and following overexertion, the patient had severe pain of constricting type over the lower substernal area with associated dyspnea, profuse sweating, and frothy sputum. Three injections of 0.25 gm. of morphine sul-

phate failed to give relief until three hours afterward. A similar attack of pain which lasted for a half hour occurred the following day, and pain of less severity was experienced for short periods daily up to the time of admission to the hospital. While in the hospital the patient continued to suffer from attacks of tightness in the thorax, associated with extreme dyspnea and a hacking cough productive of whitish sputum.

Examination of the lungs following these attacks showed the presence of abundant moist râles indicating pulmonary edema. Gradually progressive failure of the congestive type with enlargement of the liver and ascites characterized the patient's course while in the hospital, and death occurred sixty-one days after admission.

At examination on admission the systolic blood pressure was 160 and the diastolic 115. The heart measured 15 cm. in its greatest transverse diameter; its apical tones were rapid, regular, and indistinct. Examination of the fundus oculi did not reveal significant changes. The leukocyte count was 12,200. The Wassermann reaction of the blood was negative. The temperature reached a maximum of 101° F. on the second and third days following admission. The diagnosis was essential hypertension, angina pectoris with coronary sclerosis, and recent coronary occlusion with myocardial infarction. On the basis of the electrocardiographic tracings, it was possible to predict that this infarction should involve the posterior and basal portion of the left ventricle or the adjacent septum, or both, in the region usually supplied by the right coronary artery.

The electrocardiogram taken on admission was characterized by the depression of the R-T segment in lead I and its elevation in lead III (Fig. 154, *A*). The T wave in lead III, which first was slightly inverted, later became diphasic, and finally isoelectric. Subsequent electrocardiograms were characterized by a tendency of the R-T segments in leads I and III to return to their iso-electric level, although never quite reaching it (Fig. 154, *B*, *C*, and *D*). This change was presumably associated with the healing process and fibrous scar formation which was seen to be well advanced at the time the patient died. It may have

been associated also with the fact that the process of infarction extended so far toward the anterior portion of the ventricular septum, thus tending to minimize the disturbance of the isoelectric balance produced when the area of infarction is limited to the posterior basal portion of the left ventricle and the septum immediately adjacent to it.

At necropsy the heart was found to weigh 475 gm. The left ventricle was dilated, graded 2. There was a "soldier's patch"

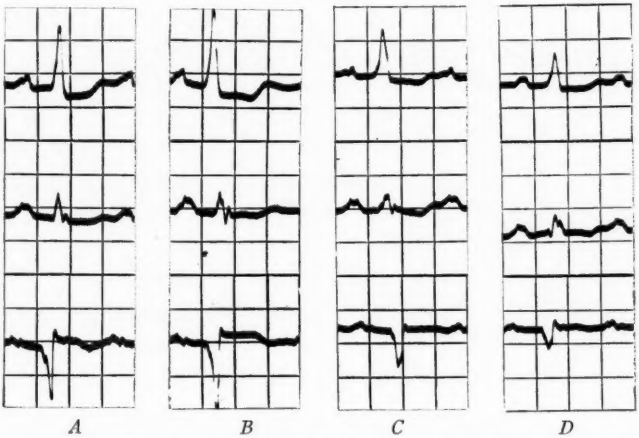


Fig. 154.—Case 3. *A*, *B*, *C*, and *D*, Electrocardiographic tracings taken the day of admission and four, seventeen, and thirty-five days, respectively, after admission to the hospital. The depressed R-T segment in lead I and the elevation of the R-T segment in lead III may be noted.

on the posterior surface of the left ventricle and a section made through this area revealed extensive scarring and thinning of the muscle, graded 3. The infarction involved the posterior basal portion of the left ventricle and the adjacent three-fourths of the interventricular septum (Fig. 155). There was aortic sclerosis, graded 3. The right and left coronary arteries were sclerosed, graded 3; their lumina were narrowed, with areas of almost complete occlusion in several portions of both. In the left anterior descending branch of the coronary artery just below the point where the circumflex branch arises, there was an old thrombus of

about 3 cm. in length which showed signs of canalization. Dissection showed that the infarcted area in the posterior portion of the left ventricle and in the portion of the interventricular septum immediately adjacent received their blood supply in the

Fig. 155.—Case 3. *CI*, Chronic infarction involving the posterior basal portion of the left ventricle and the adjacent three-fourths of the interventricular septum; *P*, posterior portion of the left ventricle; *A*, anterior wall of the left ventricle, and *IV*, interventricular septum.

usual manner from branches of the right coronary artery. The endocardium beneath the area of infarction was white and glistening, and the subadjacent muscle was thinned and showed extensive fibrotic changes.

Case 4.—A man, aged fifty-eight years, came to the clinic complaining of substernal pain following exertion. At times, this pain radiated down the left arm and was relieved by rest. Thyroidectomy for exophthalmic goiter had been performed five years previously, from which the patient had made a satisfactory recovery. Before the examinations at the clinic were

completed, at 9 p.m. he was seized by a severe agonizing pain over the substernal and precordial area which radiated to the spine and left arm, accompanied by associated dyspnea and profuse perspiration. The patient received three hypodermic injections of morphine before reasonable relief was obtained from this pain. In fact, some pain still persisted in the precordial area the morning following the attack.

The systolic blood pressure was 112 and the diastolic 64 when the patient entered the clinic. Following the severe attack of pain, the sytolic blood pressure was 80 and the diastolic 60. The leukocyte count during the first four days following the seizure rose to a maximum of 10,500; 79 per cent of the leukocytes were polymorphonuclear. An elevation of temperature of one degree occurred the second day after the acute pain in the thorax, and reached a maximum of 101.5° F. prior to the patient's death.

Two days after the first attack of pain, the patient had a second seizure of a similar type and in the same site, which again required three hypodermic injections of morphine to give relief. Dyspnea, more or less pain in the thorax, and gradually increasing weakness persisted throughout his stay in the hospital, and death from myocardial failure occurred on the seventh day. A diagnosis of coronary sclerosis with coronary occlusion and myocardial infarction was made.

On the basis of the electrocardiographic changes described, a prediction was made that the infarction involved the posterior basal portion of the left ventricle and the adjacent intraventricular septum in the region usually supplied by the right coronary artery.

The electrocardiogram taken prior to the attack of coronary occlusion did not show significant abnormalities. Tracings taken two and five days after occlusion showed the depressed R-T segment, and exaggerated T wave in lead I. The T waves in leads II and III were inverted and a slightly rounded contour of the R-T segment preceding was seen, especially in lead III.

The transitory, incomplete bundle-branch block, observed following the second severe attack of pain, led me to suspect that a second infarction had taken place. The present uncertainty

regarding the classification of bundle-branch into right and left types and their blood supply did not permit any prediction as to the site of the second infarct. As a matter of fact, as the necropsy disclosed, a second small infarct was found in the anterior portion of the left ventricle. Whether the vascular disturbance that produced this infarct accounted for the occurrence of the electrocardiographic evidence of bundle-branch block it is impossible to say.

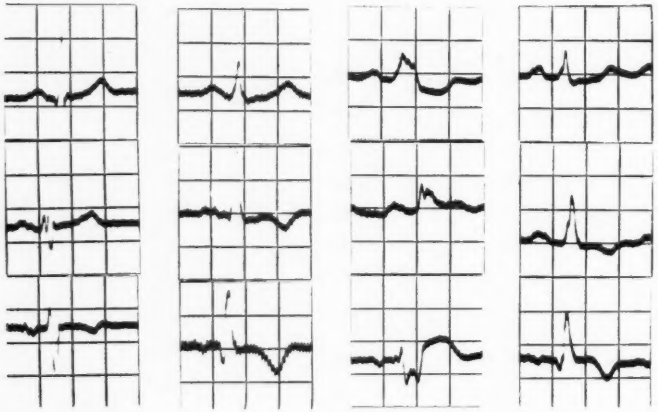


Fig. 156.—Case 4. *A*, Electrocardiographic tracing taken one day before coronary occlusion; *B* and *D*, electrocardiographic tracings taken two and five days after occlusion; the development of the depressed R-T segment in lead I and the inverted T waves in leads II and III with the characteristic rounded contour preceding them are shown; *C*, transitory incomplete bundle-branch block observed on the third day after coronary occlusion.

At necropsy, the heart was found to weigh 555 gm., and sclerosis of the aorta and of the right and left coronary arteries, graded 3, was present. The endocardium and valves appeared normal, and a thrombus occluded the right coronary artery close to the interventricular septum. A large area of infarction was found in the posterior portion of the left ventricle and in the adjacent interventricular septum. The anterior descending branch of the left coronary artery was sclerosed, graded 3, and 1 cm.

from its beginning the sclerosis was extreme, the walls of the arteries were calcareous and at this point there appeared to be a small thrombus. In the anterior portion of the left ventricle and the adjacent septum at a distance of about 1.5 cm. from the apex was another area of acute infarction about 2 cm. in diameter. This area of infarction was small as compared to that observed in the posterior portion of the left ventricle and the posterior interventricular septum.

COMMENT

Four cases are presented, in which it was possible to predict, on the basis of electrocardiographic changes, the site of myocardial infarction found at necropsy. This is possible in a high percentage of cases, owing to the fact that infarction of the anterior portion of the left ventricle and apex produces changes in the R-T or S-T segment of the electrocardiogram that are characteristically different from those obtained when infarction involves the posterior basal portion of the left ventricle. Since the left coronary artery supplies the anterior portion of the left ventricle and the right coronary artery, the posterior portion in the average heart, the localization of the region of infarction permits the identification of the left or right coronary artery as the site of occlusion, unless the vascular supply is anomalous in distribution.

In case of multiple acute infarctions occurring in the course of a few days, an electrocardiogram permitting localization of infarction may be obtained only with the first infarction. If electrocardiograms are taken following each of two infarctions, separated by a considerable interval of time, it will usually be possible to localize each infarction. There are many variations in the areas involved in infarction of the left ventricle which depend on the distribution of the artery occluded. These areas may be so distributed as to overrun the regions of the left ventricle which have associated characteristic electrocardiographic changes. This will necessitate the careful study of the electrocardiographic changes in order to see which type of typical changes are approximated, and deductions should be made on that basis. Correlation of carefully described areas of myocardial infarction

with electrocardiographic changes gives information regarding the local areas of the ventricular muscle capable of producing characteristic changes in the R-T and S-T segment, and thus furnish a basis for a much better understanding of the mechanism involved in the production of abnormalities of the T waves, and by inference a better understanding of the normal T wave. The information summarized to date in the studies of the electrocardiographic changes associated with myocardial infarction are sufficient to fulfill Herrick's prophecy in 1919 when he stated: "The thought has been that if it can be proved with a certain artery obstructed there is a definite lesion in the heart muscle or in the conducting system and if with that lesion there is a definite electrocardiogram may we not, when we encounter that abnormal electrocardiogram in the human being, particularly if he has had symptoms suggestive of coronary thrombosis, be able to state with a reasonable degree of certainty that the patient has had obstruction in a particular portion of the coronary system? May it perhaps be possible to localize a lesion in the coronary system with an accuracy comparable to that with which we locate obstructive lesions in the cerebral arteries?"

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FIBROMYOMA, SARCOMA, AND ADENOCARCINOMA IN THE SAME UTERUS

L. Mary Moench

A nun, aged thirty-nine years, registered at the clinic in July, 1929. Her chief concern was a sense of gastric flatus and distress after meals, headache, and some exhaustion which had troubled her for many years. Her trouble had increased in the last three years.

The portion of the history relative to the pelvis, given on questioning, was that there had been uterine bleeding on three occasions during the last four weeks, which she attributed to the unusual exertion incident to travel. There had been no other unusual vaginal discharge and her attention had never been directed to the pelvis by any symptoms in the past.

The patient was slightly above her average weight. There was a slight elevation of blood pressure. Pelvic examination revealed a fundus enlarged by multiple small tumors, the largest about 5 cm. in diameter on the posterior wall of the uterus. The uterus was retroverted and moderately fixed. Investigation of the gastro-intestinal tract, including roentgenologic examination of the gallbladder, stomach, and colon did not disclose evidence of disease, and the other laboratory tests gave negative results, with the exception of the blood count. Examination of the blood revealed the presence of a rather severe grade of anemia. The concentration of hemoglobin was 35 per cent. Erythrocytes numbered 3,570,000 to 3,920,000 and the leukocytes 5,600 to 5,800 for each cubic millimeter of blood. The differential count was essentially normal and a study of blood smears revealed that the anemia was of the type seen in deficiency of hemoglobin.

It was difficult to explain this anemia as resulting from loss of blood. The recent metrorrhagia had been slight and there had been no profuse menstrual flow. However, because of the presence of the uterine tumors, and the possibility of mild cholecystitis being present, it was thought best to explore the pelvis and examine the gallbladder.

The operation, performed August 8, revealed a normal gallbladder. The appendix was retrocecal and was removed. The uterus contained multiple fibromyomas, and hysterectomy was performed. The pathologist reported that one of the tumors,

Fig. 157.—Gross appearance of uterus in which were found fibromyoma, sarcoma, and adenocarcinoma.

which was entirely encapsulated, was undergoing sarcomatous change and that there was also a diffuse adenocarcinoma of the body of the uterus with an adenocarcinomatous polyp. The patient was given a vaginal pack of radium while in the hospital.

Newell, in 1928, in reporting a similar case of myoma, sarcoma, and carcinoma of the uterus remarked that it is very unusual to observe three types of neoplasm arising from the same uterus. He found only four such cases reported in the literature although there were twenty cases of carcinoma and sarcoma coexisting in the same uterus. Most of the cases were of sar-

comas arising from either the endometrium or myometrium and not sarcoma arising in a myoma. In this case the sarcoma was developing from the struma of a myoma and there were adenocarcinomatous changes going on in a polyp of the endometrium, thus demonstrating, at two points in the same uterus, the transition from a benign to a malignant growth.

SARCOMA IN UTERINE FIBROMYOMA; ADENOMYOMA OF THE ABDOMINAL WALL; COMPLETE UTERINE PROLAPSE

DELLA G. DRIPS

SARCOMA IN UTERINE FIBROMYOMA

Case 1.—A married woman, aged fifty-seven years, registered at the clinic, November 29, 1926. The family history was negative. The menstrual history was negative, and menopause had occurred uneventfully seven years before. This patient had been at the clinic twice before, in 1912 and 1923, for minor complaints. Pelvic examination at these times had revealed nothing unusual except retroversion. The chief complaint was of a dull pain in the right lower quadrant of the abdomen, which the patient stated had come on about four weeks before. The pain had been relieved when she lay down. She said that there had been much soreness all through the abdomen at times since the onset of the pain. There had been so much abdominal soreness a few days before she came to the clinic that she had hardly been able to let the physician examine her. Pain was not present at the time she was being examined in the clinic. She complained of having had much distress from gas in the stomach after meals since the onset of the pain.

General examination gave essentially negative results except for the condition in the pelvis. The uterus was globular and in anterior position. It was enlarged to about 7 cm. in diameter, with what felt like a definite irregularity anteriorly. The uterus felt soft and was fixed. A polyp extruded through the cervical os. The patient's temperature was 99.2° F. Concentration of hemoglobin was 61 per cent; erythrocytes numbered 3,800,000, and leukocytes 15,200 for each cubic millimeter of blood. A

diagnosis was made of degenerating fibromyoma, with low-grade inflammation about the tumor and a cervical polyp. Pelvic exploration was advised.

At operation, a round tumor of the uterus was found filling the pelvis. The tumor was soft. The blood supply was greatly increased, which made the surgeon feel that it was a malignant tumor. Total hysterectomy was done, with removal of the right tube and ovary. The left ovary was small and the left tube and ovary were saved. The surgeon made a note that multiple polyps projected into the cervix. The pathologist reported a sarcomatous, degenerating, hemorrhagic fibromyoma, 7 cm. long and 6 cm. wide.

Convalescence was uneventful. The patient was allowed to go home over the Christmas holidays, before the prophylactic roentgenologic treatment was given. When she returned for this, four weeks after she had been operated on, vaginal examination revealed a circumscribed mass about 5 cm. in diameter, to the left of the middle line, movable and not tender. The patient was given the roentgenologic treatment and was advised to return for reëvaluation of her condition in two months. She did not return until August 26, 1929. At this time, she complained of a lump in the right side of the neck. She said she first had noticed this two months before. It had continued to enlarge. She had felt a small lump below the growing one for more than two months. There had been some associated tenderness, but no pain. She had no other complaints except a slight cough which she had had for some time. She had not lost weight or strength. General examination revealed a node in the right upper cervical region, 4 cm. in diameter, firm but movable. There was another node below this, 1.5 cm. in diameter. Otherwise the results of general examination, including that of the pelvis, were negative. A roentgenogram of the lungs, however, disclosed extensive bilateral metastasis. The patient was given radium over the nodes of the neck and treatment by roentgen ray over the thorax.

The patient reported again, November 18, 1929. She said she felt better than she had for months. She had gained weight and her cough had disappeared. There was no evidence of new

metastasis. The cervical lymph nodes were practically unchanged. Because of her good general condition she was given more treatment by radium and roentgen ray, and was advised to report by letter in two months.

Case 2.—A woman, aged forty-two years, registered at the clinic, August 8, 1929. The family history was negative. The patient had been married at seventeen years of age and had one child fifteen years old. Menses had begun at fifteen years of age, had always been regular and had occurred every three and a half weeks. The flow had lasted from four to seven days. She stated that menstrual flow had been profuse for a time before an operation which she had had in Germany eight years before, at which time a uterine tumor had been removed. After this, menstrual flow had been normal in amount until the last one and a half years, when it had again become profuse. She felt that the uterine tumor had recurred, and came to the clinic to have the uterus removed. There had been no metrorrhagia except on two occasions when she had had a slight bloody discharge a few days after she had thought her period was over. She had had slight, yellowish leukorrhea for some time.

Pelvic examination revealed a large uterus which felt about 10 cm. in diameter; it was markedly retroverted, and fixed. It felt soft, the consistence of a pregnant uterus. It was impossible to outline a definite tumor. The cervix was soft and there was a granular erosion of the posterior lip, which bled easily. The general examination was otherwise essentially negative. Colostrum could be expressed from the breasts. The hemoglobin was 72 per cent, erythrocytes numbered 4,250,000, and leukocytes 3,600 for each cubic millimeter of blood. A diagnosis of degenerating fibromyoma in a retroverted uterus and of chronic cervicitis with the possibility of an early malignant condition was made. Total hysterectomy was advised.

Operation was performed, August 13, 1929. The body of the uterus was found to be densely adherent in the pelvis. It measured 15 cm. in diameter. Total hysterectomy and bilateral salpingo-oöphorectomy were done. The pathologist reported

fibrous and cystic cervicitis, slight hypertrophic endometritis, fibrosarcoma in a fibromyoma, graded 2, 10 cm. long, 8 cm. wide, and 7 cm. thick. There was another small fibromyoma, 5 mm. in diameter. The adnexa showed chronic inflammatory changes. Recovery from the operation was uneventful. A series of treatments by roentgen ray to cover the pelvic fields was given.

The two cases cited call attention to certain clinical distinctions in the diagnosis of early uterine sarcoma, noted many times before. The tumors in both cases were large, soft, and fixed. There was nothing definitely to distinguish them from large degenerating fibromyomas with secondary inflammatory changes occurring about them. It was not possible, in either case, to be sure that the tumor had developed rapidly, although the short duration of the symptoms in the first case was suggestive of recent growth. A malignant condition should have been suspected in this case, as the tumor had increased markedly in size and had begun to give symptoms after an uneventful menopause. Following the dictum that any uterine tumor which is soft and fixed or in which there is evidence of growth or of softening after menopause should be treated surgically rather than with radiotherapy, it is not necessary, practically, to make a more accurate preoperative diagnosis.

From the standpoint of prognosis and treatment in cases of sarcoma in fibromyoma, the first case is especially interesting. In less than two years after operation, which was followed by roentgenologic treatment, the patient returned with regions of metastasis scattered through the lungs and in the cervical nodes.

The concensus of opinion has been that metastatic involvement of other organs occurs relatively late in most cases of uterine sarcoma. Case 1, judging from the length of time that the symptoms had been present, and from the fact that the sarcoma was still encapsulated, was certainly a fairly early case. There is no doubt but that the prognosis should be very guarded in these cases and that radium should be applied in the vagina and roentgen rays to the pelvic fields as soon as is thought advisable following operation. The treatment by roentgen rays should be

repeated at intervals for several series. Fortunately, these tumors are rather rare. Masson, in 1923, published a review of a series of cases observed over a period of ten years in The Mayo Clinic. Four thousand three hundred twenty-two patients were operated on for uterine fibromas and in only forty-four (1 per cent) was sarcoma found. Other authors have given much higher percentages, from 4 to 10 per cent. In the year from October 1, 1928, to October 1, 1929, there were 541 patients operated on for uterine fibromyoma. In seventy-five of these cases the tumors alone were removed. In 466, the uterus was removed. In only three cases was sarcoma present in a fibromyoma, which makes the proportion for the year only 0.55 per cent. Case 2 is one of these three cases and the case reported by Dr. Moench, in this issue, is another.

ADENOMYOMA OF THE ABDOMINAL WALL

Case 3.—A negro woman, aged thirty-three years, registered at the clinic, August 26, 1929. She had been married ten years, had never been pregnant, and had not used contraceptive measures. Her menses had begun at the age of thirteen years, had been regular and had occurred every four weeks. The periods had lasted only three or four days and the flow had been moderate. She had noticed slight leukorrhea for some time. Her chief complaint was pain in the region of the umbilicus, which had come on after every menstrual period for the last two years. It usually had lasted seven to ten days. The patient had noticed that, during the period of the pain, there had been a tender, firm area around the umbilicus. The pain had been dull usually, but occasionally it had been "piercing." She described her trouble as "stomach trouble and not indigestion." There had been no associated nausea or vomiting. She complained secondarily of rather severe constipation for relief of which daily catharsis had been required. She complained also of much distress from gas throughout the abdomen. The latter, she said, was present all the time, whereas the pain about the umbilicus was present only following the menses.

General examination revealed a very large, irregular, firm

tumor filling the lower half of the abdomen. Just above, and seemingly attached to the umbilicus, was a firm, tender mass about 4 cm. in diameter. It was definitely attached to the skin. The patient said this was the region of the pain of which she complained. Pelvic examination confirmed the impression that the tumor palpated in the lower part of the abdomen was an enlarged and irregular tumor of the uterus. A diagnosis of multiple uterine fibromyoma with an adenomyoma of the umbilicus was made and operation was advised.

The patient was operated on, August 31, 1929. The uterus was found to contain multiple tumors making a mass the size of a uterus at five months' gestation. Subtotal hysterectomy was done, with removal of both tubes and the left ovary. The right ovary apparently was normal and was saved. An adenomyoma, apparently of the abdominal wall just above the umbilicus, was removed. The pathologist reported the latter as a subcutaneous nodule, 3 cm. in diameter, made up of inflammatory adenomyomatous tissue. The convalescence was uneventful.

The unusual situation of this adenomyomatous tissue makes this case worth reporting. The patient had not had abdominal operations which might have made possible the implanting of the endometrial tissue. The origin of a subcutaneous nodule made up of tissue microscopically similar to endometrium and apparently affected by the ovarian hormones, in such a situation is not completely explained by any of the existing theories. Sampson's theory of transplantation may eventually explain such misplaced endometrial tissue. He stated: "If fragments of endometrial tissue escape into the venous circulation of the uterine wall during menstruation and become implanted on the endothelial surface of the veins and venous sinuses of that organ and if a similar condition arises in veins about misplaced endometrial cavities in the vagina, it is natural to assume that a like implantation of this tissue might occur in veins remote from the endometrial cavities. This might account for the origin of misplaced endometrial tissue at a distance from the uterus, such as some of those in the vagina, vulva, groin, or even the umbilicus, the latter through the round ligaments and epigastric veins."

In 1926 I reported a case of adenomyoma of the umbilicus in a young negro woman. In that case, also, the adenomyoma was associated with multiple uterine fibromyoma.

COMPLETE UTERINE PROLAPSE

Case 4.—A married woman, aged fifty years, a housewife, registered at the clinic September 25, 1929. She had been married twenty-nine years and had had two children and one miscarriage during the early period of her married life. Menstruation had begun at the age of fifteen years. Her periods had been regular and had occurred every four weeks, except that she had missed the period previous to her registration. The period always had lasted seven or eight days, and had been associated with a bearing-down pain, at times severe enough to keep her in bed for a day. The flow never had been profuse. She was menstruating on the day of the examination. Her chief concern was a uterine prolapse. She said that she had known, for years, that the uterus was lower than it should be, but it never had given her any discomfort until seven years before. Until four years before admission, she had been able to replace it, but since this time she has not been able to replace it even at night. She had worn a pad constantly to protect the uterus as much as possible and because of a white vaginal discharge. She said she had done all her own work, still attended all the lodge dances, and danced her share without much discomfort. She had no trouble referable to the bladder and the bowels were regular. She had no other complaint except a goiter, which she had had for thirty years.

The general examination was negative, except for infected tonsils and a large, adenomatous thyroid gland. Examination of the pelvis revealed complete prolapse of the uterus and vagina (Fig. 158). The uterus felt enlarged and firm, as if it contained a fibromyoma. There was much thickening of the vaginal mucous membrane and much hypertrophy of the cervix, with two areas of ulceration, about 2 cm. in diameter, on the cervical lips. A polyp extruded from the cervical os.

The patient was advised to return home for a time, until the menstrual period was over, to stay off her feet, and after the flow had ceased, to apply a hot dressing of boric acid to the prolapsed mass twice daily until she returned. She did not return for one month, as the menstrual period did not stop. She had not applied any hot dressings. This was the first prolonged period of flow she had had. Catheterized urine contained pus, graded 3, and there was 10 c.c. of residual urine. The return of phenol-

Fig. 158.—Case 4. Complete uterine prolapse.

sulphonephthalein, from both kidneys taken together, was 40 per cent in two hours.

The patient was operated on, November 1, 1929. A Mayo vaginal hysterectomy and partial vaginectomy were done. A large fibromyoma was found in the posterior wall of the uterus. The bladder was found to be completely outside the body, the urethra pointing downward toward the anus. The tissue was like leather. The uterus and nearly all of the vagina, except a strip 2.5 cm. wide extending around the vaginal outlet, were re-

moved. The bladder was replaced and fixed in position. The pathologist reported multiple uterine fibromyomas (the largest 4.5 cm. in diameter, and the smallest, 1 cm.), hypertrophic endometrium, chronic cervicitis, and chronic ulcerative vaginitis.

The convalescence was essentially uneventful and the patient was dismissed November 20, 1929.

OBESITY

CLIFFORD J. BARBORKA

THE apparent paradox that certain persons get fat and others do not on what appears to be equivalent diets invites much speculation. The old classification of exogenous obesity attributed to inactivity and overfeeding, and endogenous obesity, or the constitutional type, for which a variety of physiologic and pathologic functions has been ascribed, is subject to attack on the basis of Newburgh's contention of obesity, namely, that the subject takes in more than is used up regardless of any disease or any inherited tendency which may be present.

There can be no doubt that obesity is often the result of overindulgence in food and lack of exercise. There are persons, however, who gain weight on what appears to be a moderate intake of food, or even a restricted intake, and who indulge in considerable exercise. In many instances there seems to be an hereditary background as though there was a constitutional tendency to obesity. Many common factors may be observed in the accumulation of evidence of the incidence of the development of obesity. In many cases obesity develops following lactation because of the fact that the young mother in her zeal to supply adequate nourishment for her baby overeats and pushes fluids to a maximum. It is common for obesity to follow convalescence from operation or from prolonged illness. There are natural periods of alterations of flesh which tend to occur at certain physiologic epochs, as puberty, menses, pregnancy, and menopause.

The problem of obesity in its many aspects has been receiving more attention in recent years and is becoming a significant factor

in clinical practice. One of the chief reasons that bring most obese women to the physician is the lack of grace and beauty of figure which, in turn, is likely to bring about certain psychic effects. As a matter of fact, the final impetus that brings the obese person to the physician is one of the sequelae of obesity rather than the esthetic considerations. Certainly it is the adverse effect on longevity and the predisposition to secondary pathologic changes that should concern the physician. The medical actuarial tables on mortality statistics quickly point out the effects of obesity on the duration of life. The per cent ratio of actual to expectant death of overweight men and women increases proportionally to each 10 pounds of overweight. This fact is recognized by insurance companies, who regard obesity as a serious impairment, and the obese person who desires life insurance has his rate increased considerably because of the extra risk associated. Not alone does the obese individual have a physical and economic handicap, but the abnormal adiposity predisposes to other pathologic conditions. Joslin has emphasized the relation of obesity to diabetes. He found that 70 to 85 per cent of persons with diabetes gave a history of obesity. If there is a latent tendency to diabetes the development of obesity certainly seems to precipitate glycosuria. It is surprising how often the history of obesity is present at the onset of glycosuria. Furthermore, the carbohydrate metabolism seems to be altered, as 40 to 60 per cent of all obese persons have an abnormal glucose tolerance. Foster stated that 50 per cent of patients with hypertension are obese. A large proportion of patients with cholelithiasis are overweight. The development of cardiac embarrassment is likewise a common observation. There also are many minor difficulties, such as varicosities, excessive perspiration and eczema, that arise from obesity. The surgeon is well aware of the poor surgical risk and the possibility of postoperative hernia and a tendency to pneumonia. Many orthopedic problems are aggravated or precipitated by overweight. It has long been known that a certain relation exists between obesity and complete or partial sterility. Some authorities feel that obesity is an exciting cause of sterility although other facts

suggest that sterility is primary and that obesity supervenes as a result of metabolic disturbances produced by the elimination of the reproductive functions.

From this brief review it is apparent that obesity, regardless of the mechanism by which it may be produced, from a simple gain of 10 to 20 per cent above the normal weight for a certain height, sex, and age, up to vertiable monstrosity, should be considered pathologic.

Various endocrine dysfunctions are accompanied often by different types of adiposity and certain regional distributions and peculiar configurations. One of the most characteristic symptoms in the dystrophia adiposogenitalis is obesity. The particular portion of the pituitary gland which is concerned in the development of obesity is open to question. Whereas the obesity may be general in pituitary lesions, it usually has fairly definite types of distribution in which deposits of fat are localized chiefly about the hips, the upper part of the thighs, the mons veneris, the lower part of the abdomen with its apron, and frequently the breasts.

Two general groups are commonly seen. In one group, especially women, there is an enormous preponderance of fat localized about the hips, lower part of the abdomen and upper part of the thighs (Figs. 159 and 160), and the remainder of the body being fairly normally developed. This has been often referred to as the girdle type of obesity. In the other group the deposits of fat assume a more general distribution (Figs. 161, 162, and 163), a form recognized as a familial type of obesity. Attention has been called to the influence of various physiologic epochs, puberty, pregnancy, and menopause, on obesity. It often happens that at these periods the pituitary gland undergoes changes and early symptoms may develop so that delayed puberty with obesity, obesity and amenorrhea following pregnancy, and obesity, sluggishness, and headaches following the menopause, all are points to be borne in mind in the presence of obesity. There are many variations of adiposity, atypical forms of hypopituitarism, early cases, milder types, and pluriglandular varieties.

I shall present five cases of obesity that fall into the groups of girdle and familial types.

REPORT OF CASES

Case 1.—A woman, aged thirty-one years, came to the clinic because of continued gain in weight in spite of efforts at reductions. She had no other complaints. In 1921, she had weighed about 150 pounds, and in 1923, 178 pounds. At this time the basal

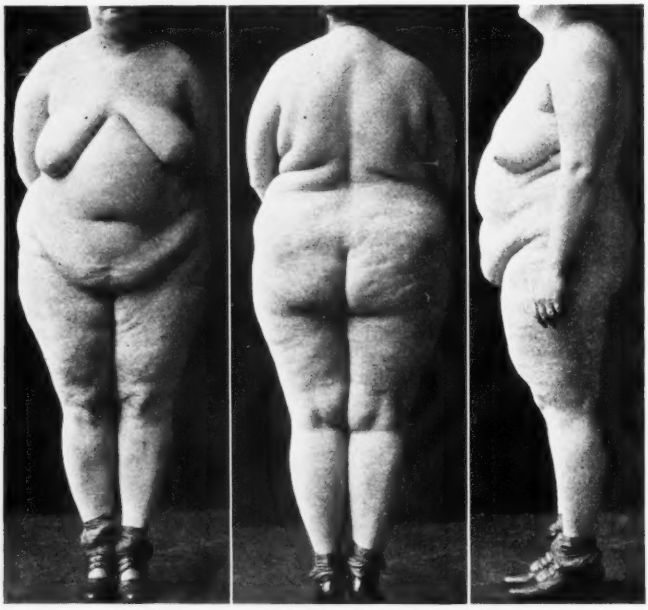

Fig. 159.—Case 1. Girdle type of obesity.

metabolic rate was −5 per cent. In 1925, she weighed 190 pounds, in 1927, 197 pounds and in 1928, 214 pounds. Since this time she had gained to her present weight of 237 pounds. Her height was 5 feet, 4.5 inches. She had been in various parts of the country, had been given various tests, and had made every effort to reduce her weight. Glandular products had been given without satisfactory results. The patient was confident that diet

would be of no benefit as she had been on a diet of less than 1,000 calories for three weeks at a time without losing weight. There was no family history of obesity. She had married in 1920 and had had twins in 1921. From this time on her weight continued to increase. She had begun menstruating at the age of fourteen years; menstruation had been normal. Her husband died in 1923.

General examination was negative except for obesity of the girdle type (Fig. 159). The systolic blood pressure was 126 and the diastolic 70. The Wassermann reaction of the blood, the blood count, and the urinalysis were negative. The basal metabolic rate was +2 per cent. The ocular fundi and visual fields were normal. Roentgenograms of the thorax and sella turcica were negative. The glucose tolerance test was negative. The patient was placed on a reduction regimen of 1,400 calories with increased exercise, and lost in six months' time approximately at the rate of 1.5 pounds a week, a total of 38 pounds. She will be kept at this weight for a period of two or three months when reduction will again be attempted.

Case 2.—A woman, aged twenty-five years, came to the clinic because of obesity and amenorrhea. She weighed 4.5 pounds at birth and at the age of six years had begun to gain weight excessively. She was plump at the age of eight years and was fat at fourteen, with a continued gradual increase in weight up to 250 pounds—her present weight. She stated that she did not eat much although she was fond of sweets and starches. She had taken various glandular extracts to reduce, but without help. In 1923 she had had 10 pounds of fat excised from the abdomen in an effort to reduce, but it came back soon. There was no family history of obesity. She had begun to menstruate at the age of fourteen and since that time had menstruated normally, but only once or twice every year. During the last two years she had had frontal and occipital headaches, especially aggravated when she used her eyes much. For the last month, she had noted some frequency, and burning on urination.

General examination was essentially negative except for a

girdle type of obesity (Fig. 160). She was 5 feet, 2 inches in height. The uterus was normal in size, but retroverted; the adnexa were normal. There were a few varicose veins of the upper part of the thighs. The systolic blood pressure was 120, and the diastolic 82. The Wassermann reaction of the blood and the blood count were negative. A catheterized specimen of urine revealed some pus cells. The phenolsulphonephthalein

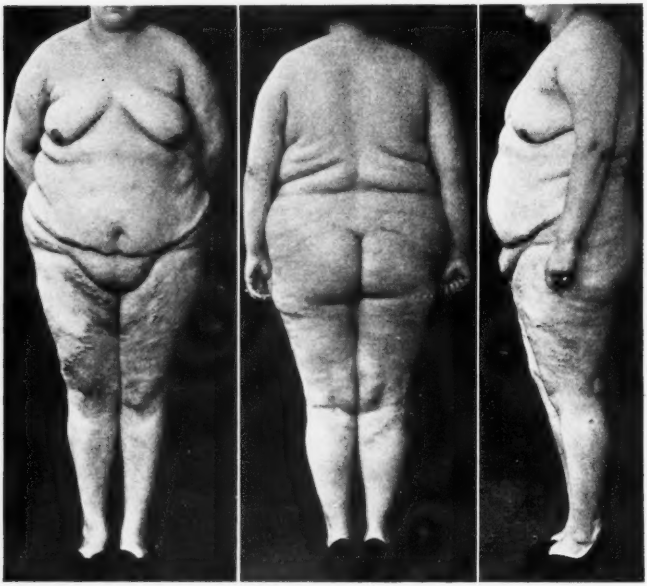

Fig. 160.—Case 2. Girdle type of obesity. Scar of previous lipectomy.

test showed a return of 55 per cent. The ocular fundi were normal. Refraction revealed compound hyperopic astigmatism. The visual fields were normal. The basal metabolic rate was +2 per cent. Roentgenograms of the kidneys, ureters, bladder, thorax, and sella turcica were negative. A cystoscopic examination was negative except that it revealed mild diffuse cystitis.

The patient was placed on a reduction regimen of 1,350 calories and increased exercise. She lost 20 pounds in two months.

Case 3.—An unmarried woman, aged fifty years, came to the clinic because of obesity and lameness of the left knee. The patient had been heavy since the age of eight years. At sixteen years she weighed 175 pounds. She now weighed 259 pounds. She had thought that she was always unusually fat about the hips, lower part of the abdomen, and the thighs. She had always had a good appetite and enjoyed her food, but did not eat as much as she could eat, or as much as she really desired. Menses

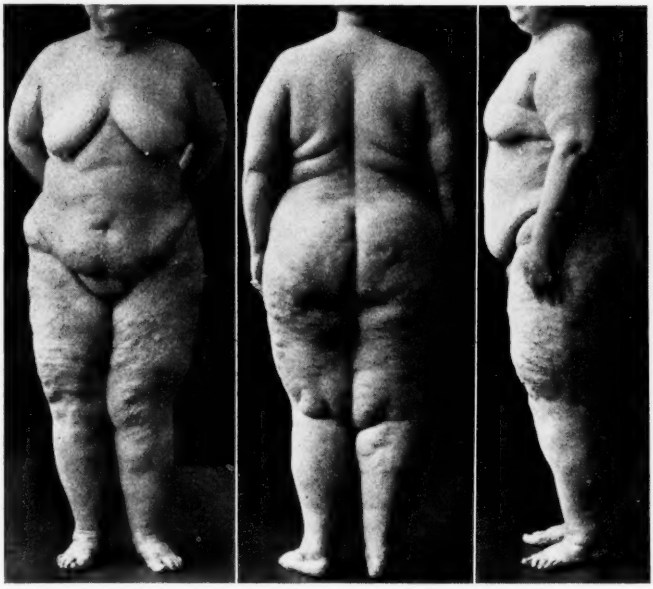

Fig. 161.—Case 3. Familial type of obesity.

had begun at the age of twelve and had been regular until the menopause which occurred at the age of forty-nine years. She had attempted reduction many times, but without results. She had bruised her left knee in 1928 and it had been lame and sore ever since.

General examination was negative except for the familial type of obesity (Fig. 161). The knee was freely movable; there

was no crepitus, but some pain on motion. The systolic blood pressure was 150 and the diastolic 92. The Wassermann reaction of the blood was negative. The blood count and urinalysis were negative. The basal metabolic rate was −1 per cent. The ocular fundi were normal and the visual fields were normal. The roentgenograms of the sella turcica and of the hands were negative. The test meal and roentgenogram of the stomach gave negative results. The left knee revealed marked hypertrophic arthritis with loose bodies in the joint. The glucose tolerance test was negative. The patient was placed on a reduction regimen of 1,200 calories, and after five months reduced her weight to 219 pounds, an average reduction of 2 pounds a week.

Case 4.—A woman, aged twenty-two years, came to the clinic because of obesity and headache. She had been told that she had pituitary obesity. There was no family history of obesity. The patient had weighed 12 pounds at birth; she had always been fatter than other children, and very good natured. At the age of twelve she weighed 163 pounds, at fifteen, 215 pounds, and at seventeen, 185 pounds. Between fifteen and seventeen she grew in height considerably, and her weight changed somewhat. At the age of twenty years she weighed 240 pounds. At the time of admission she was 5 feet in height. She had tried every type of reduction program without satisfactory results, but had remained on any one program only from two to four weeks, then became disheartened and depressed, and gave up effort. Later she was told by physicians that diet alone would never reduce her weight. She was on one accurately weighed diet of 1,200 calories in an institution and gained several pounds in two weeks. Her mother and sister had had migraine. She had had periodic headaches ever since she could remember. Menstruation had begun at twelve years and it had been normal.

The general examination was negative except for a familial type of obesity (Fig. 162), with large abdominal apron over the mons veneris. The systolic blood pressure was 128 and the diastolic 84. The Wassermann reaction of the blood, the blood

count, and the urinalysis were negative. The basal metabolic rate was 0 per cent. The ocular fundi were normal and the visual fields were normal. A roentgenogram showed the sella turcica to be moderately large, but without erosion. The neurologic examination demonstrated the central nervous system to be objectively normal.

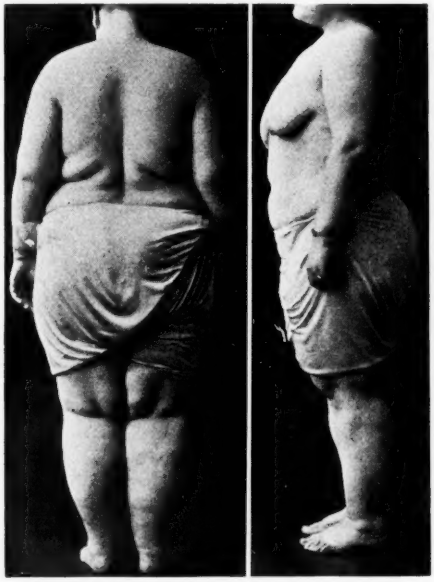

Fig. 162.—Case 4. Familial type of obesity.

The patient was placed on a 1,200 calorie reduction regimen and after a period of eighteen days she began to lose weight. With much encouragement and perseverance she lost 50 pounds in step-like fashion to the present weight of 190 pounds after five months. She was then placed on a maintenance diet, to be held at a constant weight for three or four months.

Case 5.—A girl, aged nineteen years, came to the clinic because of obesity. There was no family history of obesity. She

had been a normal baby, weighing 7 pounds at birth. She began to gain weight excessively at the age of ten years, and had gained steadily until she weighed 285 pounds. She had gracile, tapering fingers, the so-called "pituitary" hands. Her skin was delicate in texture; her complexion was fair. She did not have headaches, polyuria, or thirst. She had never been on an accurate reduction regimen. Her menstrual periods had begun at the

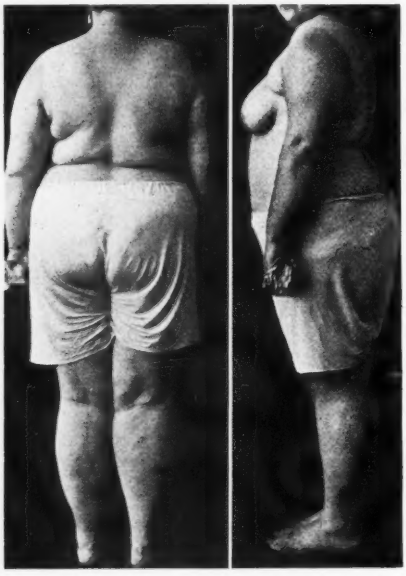

Fig. 163.—Case 5. Familial type of obesity.

age of twelve years and were normal until eighteen months before admission, when they stopped. Secondary sex characteristics were definite and sexual infantilism was not present.

General examination was negative except for a familial type of obesity (Fig. 163). The systolic blood pressure was 110 and the diastolic 70. The Wassermann reaction of the blood was negative. The results of the blood count, differential smear, and urinalysis were negative. The basal metabolic rate was −10

per cent. The ocular fundi were normal. The roentgenogram of the sella turcica was negative and a glucose tolerance test was negative.

The patient was placed on a reduction regimen of 1,000 calories for fourteen weeks, during which time her weight reduced in step-like fashion from 285 pounds to 227 pounds, a loss of 58 pounds, an average of 4 pounds a week. At this weight she was placed on a maintenance diet for four months and at present is on her second reduction regimen with 180 pounds as the objective.

COMMENT

These five cases of obesity have been presented as examples of two types of configuration commonly seen. The distribution of fat and the history of symptoms suggest at the first impression the possibility of endocrine disturbances. Yet it is not possible to classify any one of these five cases as a definite endocrine disease, and in all cases the condition responded to dietetic treatment.

The underlying principles of all reduction regimens are simply the maintenance of nitrogen equilibrium with restriction of calories lower than the needs of the body. Thus the fat of the body is called on to make up the deficiency. It is important to plan the arrangement of the proportions of carbohydrates, proteins, and fat in the reduction diet so that the actual metabolizing mixture of food given by mouth and of tissues of the body that are oxidized to make up the deficiency of calories be properly balanced. To do this, from 0.67 to 1 gm. of protein for each kilogram of the expected weight is set as an objective. The total estimated calories for this expected weight is then estimated by allowing 25 to 30 calories for each kilogram. The carbohydrate and fat are then arranged so that the total fatty acids and glucose values will approximate a 1.5 to 1 ketogenic-antiketogenic mixture. Having thus established the amount of carbohydrate, protein, and fat for a normal metabolizing mixture for the expected weight, the carbohydrate and protein amounts are left as calculated and the fat is reduced to the number of calories adequate for the patient. The reduction allowance from 750

calories to 1,400 calories daily is varied, depending on the type and degree of obesity and the patient's tolerance to loss of weight. The amount of exercise can be increased to meet the situation. There is no reason to restrict water greatly unless obesity is complicated by a disease in which limitation of water may be desirable. It is best to reduce weight gradually by prolonging the period of dieting which is of advantage in that it accustoms the patient to a small amount of food, so that he is not so likely to overeat after the weight has been sufficiently reduced. Also slow reduction avoids the chances of weakening the patient.

On such a program, by insuring a normal metabolizing mixture regardless of the calories given by mouth, the patients do not experience clinical discomfort after the first few days. Diets as low as 750 calories can be arranged with adequate vitamins, minerals, and salts. The "endocrine obesity" yields to this procedure as well as the simple obesity without the aid of glandular products. It is known that although a patient on a reduction diet is actually oxidizing tissue, the scale may not show loss and may even show a gain for days, because water is retained to replace the fat burned. Then all at once diuresis takes place and a rapid loss follows. The step-like fashion of reduction has been observed by both laymen and physicians.

The chief cause of failure in the treatment of obesity, at least of the simple forms, has been the lack of perseverance and courage to follow a restricted regimen long enough to overcome this tendency on the part of the water to be retained by the tissues to compensate for the fat oxidized.

Physicians cannot be too strongly cautioned against promiscuous and indiscriminate use of thyroid gland in the treatment of obesity, especially by the laity. The use of thyroid extract outside of the well-controlled advice of a physician is pernicious as it frequently leads to material cardiac injury when taken for long periods or in too large doses. If the physician can observe patients daily and can make frequent tests of basal metabolism it aids materially in reducing weight rapidly, and under certain conditions may be safely employed.

Fashion in recent years has decreed that the figure of women

should be slight and sylph-like. To conform to this many women have attempted, on their own initiative, many ridiculous dietary measures, and not infrequently this has led to extreme undernutrition, ill health, and even death. It is the physician's duty to point out limits of reduction and that health is more to be desired than a fashionable figure.

CONCLUSIONS

The problem of obesity is difficult to solve perhaps because, as Du Bois has stated, there is no stranger phenomenon than the maintenance of a constant body weight under marked variation in bodily activity and consumption of food. Few scientific data are available to explain maintenance of normal weight. Many factors, such as disturbance of endocrine glands, water metabolism, specific dynamic action, and fluctuations in basal metabolism, have been held responsible. Such data as Newburgh has recently presented in determining the total heat elimination and total water exchange, with accurate studies of the nature of obesity, do not lend support to the conception of a mysterious economy practiced by the tissues infiltrated with fat.

Obesity can and does occur in patients without showing clinically any direct relation to intake of food. Whatever the mechanism of obesity may be, the clinical fact remains apparent that two persons on the same intake may vary in response, one getting fat and another remaining thin. My experience has led me to believe that underweight in the otherwise healthy person also occurs even when the intake of calories is more than sufficient to supply the demands for energy. The so-called "constitutionally" obese person and the healthy person who is underweight may present extremes of the same problem.

The difference between the so-called "exogenous" and "endogenous" types of obesity is only one of degree, not of kind, and both are the result of disordered metabolism which, in the last analysis, is probably due to some glandular dysfunction which alters the previous relation between intake of food and expenditure of energy.

FISTULA BETWEEN THE ESOPHAGUS AND THE TRACHEOBRONCHIAL TREE

HERMAN J. MOERSCH

FISTULAS between the esophagus and the tracheobronchial tree are relatively infrequent, but, when present, are extremely distressing and usually are fatal. Within recent years a considerable amount has been written regarding their presence in newly born infants, and an ever increasing number of cases have been reported in the literature since the attention of obstetricians and pediatricians has been aroused to the possible occurrence of such fistulas. Congenital fistula between the esophagus and the tracheobronchial tree manifests its presence with the first effort at swallowing, and practically always causes death by the end of the second week of life, in spite of medical or surgical intervention. Symptomatically, strangulation on attempting to nurse, in newly born infants, should direct attention to the possibility of a congenital abnormality. The possibility of cardiospasm should be kept in mind, but it can readily be differentiated from other conditions by roentgenographic examination.

Little attention has been paid to fistula between the esophagus and the tracheobronchial tree attributed to other causes than those of congenital abnormality. Text-books which do refer to the subject pass it by with the statement that this condition occurs most frequently secondary to carcinoma of the esophagus. Syphilis, tuberculosis, and trauma from an impacted foreign body in the esophagus also are mentioned as possible etiologic factors.

From 1916 to 1930, seventeen patients with fistula between the esophagus and the trachea, or between the esophagus and bronchi, due to other causes than congenital abnormality, were

examined at The Mayo Clinic. In the tabulation, I have listed the etiologic factors and the number of cases due to each cause.

Carcinoma of the esophagus, as might be expected, accounted for over half of the cases reported. Considering the frequency of carcinoma of the esophagus and the proximity of the esophagus to the trachea, it is suprising that more were not seen. The fact that death usually ensues very shortly after the development of fistula that is secondary to carcinoma of the esophagus, may ac-

Fig. 164.—Fistula between the esophagus and trachea, caused by carcinoma.

count for the small number of patients that have come under observation at the clinic. In those who were seen, the condition developed only while the patient was on his way to the clinic or while he was undergoing observation. I am certain that the incidence of fistula in carcinoma of the esophagus must be much larger than the number of cases here reported would lead one to believe.

The duration of time that the carcinoma has existed, as close as one can determine from the clinical history, has no relationship to the possibility of formation of a fistula. The shortest history of carcinoma in the esophagus before the formation of a fistula was two and a half months; the longest, was twelve months.

The fistula between the esophagus and the tracheobronchial tree is not necessarily direct, but may follow a very tortuous path, as was demonstrated by the observations at necropsy in one of the cases. The carcinoma had ulcerated into the mediastinum and a large mediastinal abscess had formed, with a secondary fistula passing from the abscess into the trachea. Still another fistula had burrowed into the substance of the lung. Figure 164 is that of a fistula between the trachea and esophagus, due to carcinoma of the esophagus.

The cause listed in the two cases as being due to tuberculosis may be subject to doubt, for microscopic confirmation was lacking. However, one of these patients died at home, and the observations at necropsy seemed definitely to substantiate the conception that the fistula was caused by tuberculosis. In these cases, the history and roentgenographic examination gave evidence that was typically indicative of fistula between the esophagus and trachea. Both patients had active pulmonary tuberculosis with bacilli of tuberculosis in the sputum.

In the patient with actinomycosis, the course was unusual. A complete report of this case has been published by Vinson and Sutherland. Briefly, there was a history of long and chronic involvement of various organs of the body, apparently by actinomycosis, with subsequent development of a fistula between the trachea and esophagus. The actinomyces were readily demonstrated in smears taken from sinuses of the thorax.

The most interesting case of the entire series referred to the patient in whom the fistula was caused by a traction diverticulum. The patient was a woman, aged thirty-one years, in whom the symptoms of fistula between the esophagus and the bronchial tree dated back eight years. Four years later the diagnosis definitely was confirmed by esophagoscopic examination. The fistula at that time was reported as communicating between the lower

end of the esophagus and the bronchus of the lower lobe of the right lung. At the time the patient came to the clinic she coughed out a good portion of the food she ate. On roentgenographic examination of the esophagus after a mixture of barium had been introduced, a diverticulum of the lower third of the esophagus, with a fistula running into the bronchus of the lower lobe of the

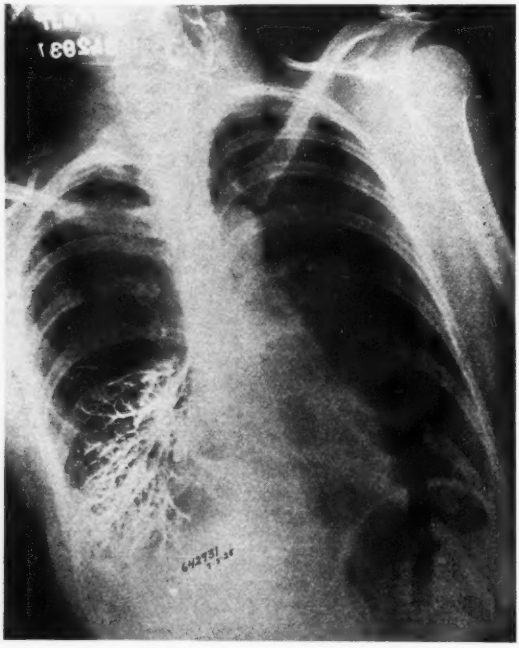

Fig. 165.—Fistula between the esophagus and a bronchus, caused by traction diverticulum of the esophagus.

right lung was reported (Fig. 165). Esophagoscopy and bronchoscopy confirmed this diagnosis. The patient was operated on, and a traction type of diverticulum with a fistula opening into the lower lobe of the right bronchus was found. The fistulous tract was excised and closed. Following operation the patient unfortunately died from pneumonia of the left lung, the

lung which was not involved in the operation. The site of operation was found to be in excellent condition, and perfect closure of the fistula had been effected. In this case, the condition was looked on as being caused by a traction diverticulum, perhaps due to tuberculous nodes and secondary ulceration into the bronchus of the right lower lobe, with formation of a fistula. Although it was assumed that tuberculous nodes were the underlying cause, the diagnosis was not confirmed, either microscopically, or surgically.

In the series there was but one case due to trauma. The condition was one of cicatricial stricture of the esophagus in a boy, aged four years, who had ingested lye four months preceding his examination at the clinic. The fistula appeared following dilatation, and the case terminated fatally. The formation of a fistula between the esophagus and the tracheobronchial tree as the result of an impacted foreign body in the esophagus and consequent ulceration through the wall of the esophagus and trachea is frequently mentioned in the literature. One patient under my observation died from mediastinitis before the process could completely occur. A child who had swallowed a five cent piece, which lodged in the upper end of the esophagus, was referred to the clinic four days after the accident. On examination the nickel was thought to have perforated the esophagus. External esophagotomy was performed, following which the coin was found to have perforated the esophagus and was seen lying against the trachea. The coin was removed and the esophagus was closed, but because of leakage mediastinitis developed and the patient died. At necropsy, an ulcerated area was found on the trachea, and if the process had been permitted to proceed, perforation and the formation of a fistula undoubtedly would have occurred.

The patient in whom a fistula developed subsequent to cicatricial stricture of the esophagus, and in whom there was a superimposed carcinoma presented a most interesting history. The patient, a woman, had had dysphagia for thirty-seven years. Twenty-five years before she came to the clinic, there had been a suggestive history of a fistula occurring following dilatation of

the esophagus, but complete recovery had followed. Treatment at the clinic was followed by fair success. However, four weeks after the last dilatation a fistula developed and the patient subsequently died. At necropsy, a carcinoma was found in the cicatricial stricture at the site of the fistula.

There were two patients, in whom the origin of the fistulas was unknown. In one syphilis was the cause suspected, and carcinoma was suspected in the other. However, the evidence in both cases was so indefinite and uncertain that the condition was classed as being of unknown origin.

Although syphilis is mentioned as a frequent cause for fistulas between the esophagus and trachea or between the esophagus and bronchi, I have not encountered a case that could definitely be thus classified. I have seen an aneurysm of the aorta that had perforated the esophagus as well as the bronchus, thereby establishing a fistula indirectly, but terminating as soon as it had formed. The Wassermann reaction of the blood in this case gave a negative result and no evidence of syphilis was seen at necropsy.

Although fistulas of congenital origin usually terminate fatally within the first weeks of life, those which occur at a later age and are of organic or traumatic origin may run a varied and protracted course. One of our patients with a fistula lived for eight years that we know of, and died as a result of pneumonia following operation, although she had had rather severe hemorrhages which induced her to seek surgical interference. Another patient gave a history, with recovery, of a fistula between the esophagus and trachea as a result of instrumentation. She had been free of difficulty for twenty-three years before recurrence took place.

COMMENT

It is a usual teaching that the mediastinum and periesophageal tissues possess little power to combat infection, but the more I see of conditions such as the formation of fistulas between the esophagus and trachea, and between the esophagus and bronchi, and of mediastinal abscesses with recovery, the more I feel that

the combative and protective powers of the mediastinum have been greatly underrated.

The condition that most closely resembles a fistula between the esophagus and trachea is bulbar palsy, with loss of the pharyngeal reflexes. Careful roentgenologic examination will permit differentiation of the two conditions. The localization of fistula by means of endoscopic examination is, however, the most accurate method of diagnosis.

TABULATION

Fistulas Not Congenital in Origin

Cause.	Cases.
Carcinoma of esophagus	9
Tuberculosis	2
Actinomycosis	1
Traction diverticulum	1
Dilatation of cicatricial stricture	1
Carcinoma in a cicatricial stricture	1
Cause unknown	2
Total	17

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PERINEPHRITIC ABSCESS

WILLIAM M. SMITH AND NORMAN M. KEITH

THE following case is presented because of several unusual features, and also to direct attention to the difficulty of accurate diagnosis in some cases of perinephritic and subphrenic infection. Perinephritis may be defined as an extension of renal inflammation into the surrounding tissues; when such a process becomes purulent, the condition is spoken of as perinephritic abscess. The condition is usually manifested by symptoms of sepsis, pain, tenderness, and a mass in the region of the kidneys. The diagnosis of perinephritic abscess is based on urinary symptoms of infection, pain which tends to be diffuse and, owing to the proximity of the diaphragm, to increase on inspiration, tenderness over the kidney, especially over the costovertebral angle, and reflex vesical symptoms.

The patient, a man aged forty-seven years, came to the clinic January 28, 1930, complaining of weakness, cachexia, and cough, with the expectoration of white, thick, mucous material. His health had always been good until September, 1929, when he had had an infection (carbuncle or furuncle) about the right knee; this was followed by severe chills and fever, and later by fever alone. Culture of the blood (elsewhere) in November was found to be positive for staphylococcus; a second culture two weeks later was reported to be negative. At that time a diagnosis of left pleural effusion was made, and thoracentesis was done, with recovery of 300 c.c. of clear fluid. The patient remained in the hospital for seven weeks. From the time he left the hospital in December until his admission to the clinic the urine had been analyzed several times, and many pus cells were found. Since December his condition had remained about the

same. The cough was always more productive at night, or with a change of posture, although it had never been profuse even with attempts at postural drainage. There had been no pain in the thorax until recently and this had not been severe. The patient stated that at times when he had coughed, he had vomited. His appetite had remained good, but he had lost about 65 pounds since the onset of the present illness.

When the patient was examined he was lying quietly in bed without dyspnea or painful breathing. The skin appeared pale, but actual bronze discoloration or pigmentation was not noted. The pupils were round and equal, and reacted normally. He had considerable dental infection. Results of the examination of the ears, nose, and throat were essentially negative. The heart was not enlarged; the left border measured 8 cm. and the right 2.5 cm. from the midsternal line. Cardiac sounds were of poor quality, but murmurs, rubs, or arhythmia were not noted. The aortic second sound equaled the pulmonary second sound, and neither was accentuated. Examination of the lungs showed that abnormal signs were limited to the right side of the thorax. Posteriorly over the right lung there was dulness on percussion from the apex to the angle of the scapula, and flatness from the angle of the scapula to the base. There was also absence of breath sounds from just below the eighth rib to the base, and distant breath sounds just above this region. In several areas whiffs of bronchial breathing came through. Vocal sounds were likewise nasal in quality at the base, and moist râles were heard over the area of dulness. The abdomen felt somewhat doughy; masses were not felt, and there was no tenderness or rigidity. The liver, spleen, and kidneys were not palpable. Apparently the abdomen was free of fluid. Tenderness or bulging was not noted over the region of the kidney. Digital examination of the rectum and prostate gland was negative. There was no edema of the extremities, and the reflexes throughout were apparently normal. The blood pressure was recorded as 140 systolic and 80 diastolic. There was no peripheral sclerosis. Urinalysis showed an average specific gravity of about 1.010 with a trace of albumin and gross pus. The hemoglobin (Dare) averaged approxi-

mately 56 per cent. Erythrocytes numbered 3,500,000 and leukocytes 10,000; the differential count was negative. Repeated examinations of the sputum and catheterized urine were negative for bacilli of tuberculosis. Culture of the urine showed the presence of *Staphylococcus aureus*. The Wassermann reaction on the blood and cultures of the blood were reported as negative. The blood urea was 11 mg. and creatinine 1.0 mg. for each 100

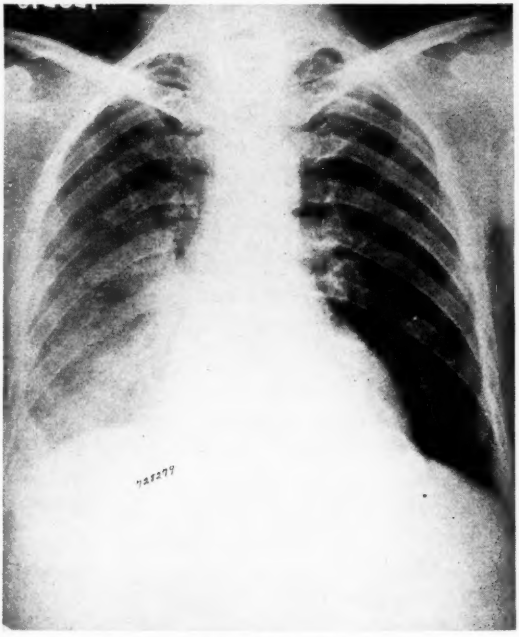

Fig. 166.—A dense shadow of the right base without elevation of the diaphragm.

c.c. Tests of hepatic function showed dye retention graded 2, and serum bilirubin of 1.1 mg. for each 100 c.c. Agglutination tests for melitensis and tularemia were negative. Roentgenograms of the thorax revealed a shadow at the base of the right lung which was variously interpreted as due to pneumonia, fluid, and thickened pleura; on one occasion an abscess was sus-

pected (Fig. 166). Elevation of the diaphragm was not noted in roentgenograms. Roentgenograms of the kidneys, ureters, and bladder were reported as negative. On one occasion a suspicious shadow was noted in a roentgenogram of the colon; a later roentgenogram was reported negative. Twenty-four hours after a barium meal a roentgenogram of the gastro-intestinal tract was also negative. Nothing of significance was noted in the electrocardiogram. The patient's temperature was not elevated.

In view of the remote history and the present persistent marked pyuria, pyelonephritis or cystitis, probably secondary to the carbuncle or to empyema, or both, was diagnosed as a probable basis of the genito-urinary condition. In view of the condition of the urine, the function of the kidney, and the absence of vesical symptoms, it was thought best first to attack the infection of the thorax. Because of the possibility of effusion or empyema in the right side of the thorax, diagnostic right thoracentesis was done February 7, 1930, and 25 c.c. of thick, creamy, foul pus was obtained. The following day aspiration of the ninth interspace on the right side of the thorax was made, with negative results. Following this, the tenth interspace at the right lower base was aspirated; 25 c.c. of pus was withdrawn, which was sent for culture and direct examination. Stains and smears failed to reveal any evidence of bacilli of tuberculosis, but a pure culture of staphylococcus was obtained. February 14, 1930, the right subphrenic space was aspirated through the tenth interspace and thick, greenish pus was obtained. The patient was immediately given an anesthetic and about 7 cm. of the eleventh rib was resected, and an abscess drained. Further exploration disclosed a large perinephritic abscess containing about 300 c.c. of thick, greenish pus. The patient improved greatly, gained in weight and strength, and was dismissed from the hospital two weeks after the operation.

This case emphasizes the difficulty often encountered in the diagnosis of subphrenic or perinephritic infections, since the only symptom that the patient had at any time referable to the genito-urinary tract was that of pyuria. Apparently the sequence of events was as follows: The infection about the right

knee in September acted as an original focus from which it is possible that septicemia from staphylococci developed, with pleural effusion on the left side of the thorax, a perinephritic abscess, and secondary right pleurisy. During the thirty-day period of hospital observation, the patient had a normal temperature, and cultures of the blood on two occasions were sterile.

THE DIFFERENTIAL DIAGNOSIS OF ASTHMA

CHARLES K. MAYTUM

ASTHMA is a disease characterized by recurrent attacks of paroxysmal dyspnea with wheezing, cough, and a sense of constriction in the thorax. Attacks are due to spasmodic contraction of the muscles in the smaller bronchi and associated turgescence of the bronchial mucosa. Asthma is apparently the result of inherent susceptibility of the bronchial muscles, the bronchial mucosa or the nervous mechanism controlling them, to stimuli which are innocuous to normal individuals, and it is quite likely that various factors are important, at different times, in the production of paroxysms, even in the same patient.

Before considering the differential diagnosis of asthma, it might be well to review some of its characteristic features. The chief symptom is dyspnea, and the two outstanding characteristics are, first, the spasmodic nature of the disease and, second, before the development of complications, the complete return to normal in the intervals. A family history of allergic disease is found in more than 50 per cent of the cases.[2, 5] The attacks tend to occur periodically and are more often nocturnal than diurnal. They may occur at the same hour of the day for long periods, or they may occur at certain seasons of the year: Asthma due to pollens occurring in the late spring, summer, and autumn months, and asthma due to infection, in the late autumn, winter, and early spring. In some instances, attacks may follow contact with certain animal or vegetable substances, or they may occur only in certain localities, or under circumstances which vary in individuals. Each attack may be preceded by certain prodromal symptoms, or there may be a sudden onset of bronchial spasm without prodromal symptoms. The attacks may

occur when the patient is seemingly in the best of health, although they are more likely to occur if the patient is physically or nervously fatigued.

Since most patients are seen for the first time rather late in the course of the disease, many of them have emphysema and chronic bronchitis which may cause more symptoms than the original attacks. A carefully taken history, however, will reveal the presence of typical features at the onset.

The appearance of the patient during an attack is characteristic. He will usually be found sitting up in bed or in a chair, supporting himself on his elbows, with his shoulders elevated, and the accessory muscles of respiration being brought into play to assist in overcoming the obstruction to his breathing. Respirations are slow and labored. The wheezy expiratory stridor may be heard at some distance and there is apparent prolongation of expiration and greater difficulty in expiration than inspiration. Cough may or may not be present during the attack; when present it is ineffectual and small amounts of tenacious glairy mucus are raised with the greatest difficulty. Speech is difficult, the words are forced out between respirations and each attempt may be responsible for several minutes of increased dyspnea. The attacks usually subside gradually with relaxation of the bronchial spasm and, as relaxation occurs, comparatively large amounts of clear frothy sputum are expectorated and, within a few hours, the patient may feel as well as ever. The thorax during attacks appears to be distended and there is very little expansile movement. The percussion note is hyperresonant, or there may be a peculiar drum-like resonance. Auscultation usually discloses many sibilant and sonorous râles throughout the lungs, although in an occasional case, one portion of the lung may be more seriously affected than the remainder. The vesicular murmur may be obscured by the musical râles which are present. Many eosinophils may be found in the sputum which is expectorated during an attack, and a relative increase in eosinophils may often be demonstrated in blood smears. Striking relief follows the hypodermic administration of epinephrine more often in asthma than in conditions which simulate it.

In most instances, the diagnosis of asthma has already been made at the time the patient is seen. The history of previous attacks of asthma or hay fever with intervals of complete relief from symptoms, the observation of the patient during an attack, and the characteristic symptoms and signs, usually make the diagnosis easy. If the attack is the first one experienced by the patient, the diagnosis is likely to be more difficult and a period of observation is often necessary before a definite diagnosis can be made. The family history of allergic disease is of assistance in many cases. In the intervals between attacks a complete and carefully taken history should be obtained and a thorough general examination of the patient should be made, including urinalysis, examination of the blood, and roentgenograms of the thorax. In certain cases, laryngoscopy or bronchoscopy will be necessary to rule out lesions in the respiratory passages. The importance of a carefully taken history cannot be overemphasized as, in most instances, it is the most valuable means of arriving at a correct diagnosis.

Since dyspnea is the outstanding symptom of asthma, practically all conditions causing dyspnea must be considered in the differential diagnosis. In the following outline an attempt has been made to group by systems the conditions which may cause dyspnea and polypnea which may be mistaken for asthma.

A. Respiratory system.
- I. Larynx.
  - 1. Laryngeal spasm:
    - (*a*) Spasmodic croup.
    - (*b*) Laryngismus stridulus.
    - (*c*) Laryngeal crisis of tabes dorsalis.
  - 2. Inflammation:
    - (*a*) Acute (acute laryngitis, diphtheritic laryngitis).
    - (*b*) Chronic (tuberculosis, syphilis).
  - 3. Angioneurotic edema.
  - 4. Paralysis of the vocal cord (Case 1).
  - 5. Laryngeal stenosis.
  - 6. Foreign body.
  - 7. Neoplasm:
    - (*a*) Benign (Case 1).
    - (*b*) Malignant.

II. Trachea and bronchi.
  1. Intrinsic lesions:
    (*a*) Acute and chronic bronchitis.
    (*b*) Chronic inflammation with stenosis (bronchiectasis, tuberculosis, syphilis (Case 3), foreign body).
    (*c*) Neoplasm:
      Benign (Case 4).
      Malignant (Case 5).
  2. Extrinsic lesions:
    (*a*) Substernal enlargement or carcinoma of the thyroid gland (Case 2).
    (*b*) Enlargement of the thymus gland.
    (*c*) Aneurysm of thoracic aorta (Case 6).
    (*d*) Tuberculous tracheobronchial nodes (Case 7).
    (*e*) Mediastinal neoplasm (benign; malignant).

III. Lung.
  1. Inflammation:
    (*a*) Pneumonia.
    (*b*) Tuberculosis.
    (*c*) Pneumoconiosis and pulmonary fibrosis (Case 8).
  2. Idiopathic pulmonary emphysema.
  3. Neoplasm of lung and pleura.
  4. External pressure:
    (*a*) Pneumothorax.
    (*b*) Hydrothorax.

B. Circulatory system:
  I. Cardiac decompensation.
  II. Coronary sclerosis (Case 9).
  III. Paroxysmal auricular flutter or fibrillation; paroxysmal tachycardia.

C. Renal system (manifested in circulatory system).

D. Nervous system.
  I. Functional air hunger.
  II. Hysterical polypnea (Case 10).
  III. Respiratory syndrome following encephalitis.

RESPIRATORY SYSTEM

Larynx.—Laryngeal obstruction causing dyspnea is usually associated with stridor and alteration of the voice. Dyspnea is both inspiratory and expiratory, more marked on inspiration, and a harsh, high-pitched stridor is present. The respiratory movements of the larynx are increased and inspiratory retraction of the structures in the neck may be marked. Cough may be croupy or harsh.

Spasmodic croup is the most common type of laryngeal ob-

struction and needs no description. Laryngismus stridulus is occasionally seen in young and poorly nourished children, and may be recognized by the peculiar crowing inspirations. In tabes dorsalis there may be laryngeal crises in which there is sudden onset of almost complete laryngeal obstruction lasting from a few seconds to a few minutes. Paralysis of the vocal cords may also occur in tabes dorsalis and cause constant inspiratory dyspnea with acute exacerbations. Other evidence of disease of the central nervous system will be found on examination. Paralysis of the vocal cord caused by pressure on the recurrent laryngeal nerves by tumors of the neck and mediastinum, or injury of the nerves following thyroidectomy, may also be responsible for dyspnea.

Angioneurotic edema of the larynx causes severe paroxysmal dyspnea and even death in some cases. Although the attack may resemble asthma in the sudden onset of symptoms, the dyspnea is characteristic of laryngeal obstruction and there is frequently a history of transient swelling of other parts of the body, more often involving the face, lips, or tongue.

If acute edema occurs in acute inflammatory lesions of the larynx, fever, toxemia, and other signs of infection are usually more prominent symptoms than dyspnea. Acute edema of the larynx may develop in cases of syphilitic laryngitis. It may develop less commonly in tuberculosis of the larynx, and cause a paroxysm of dyspnea. In these cases there is the history of alteration in the voice preceding the attack and the features of laryngeal dyspnea are present. Foreign body in the larynx or laryngeal edema from trauma following aspiration of a foreign body usually may be diagnosed from the history, although considerable difficulty may be encountered in children.

Of the tumors of the larynx, papilloma of the larynx in children is most likely to be mistaken for asthma because of the paroxysmal attacks of dyspnea which occur. Other benign tumors less commonly cause dyspnea. In epithelioma of the larynx, other symptoms are more marked and the diagnosis is usually made before the development of dyspnea.

Dyspnea associated with altered voice and inspiratory stridor

should call for a careful laryngeal examination in any case of suspected asthma.

Trachea and Bronchi.—Acute bronchitis in children may resemble asthma so closely that a rather long period of observation may be required. In most instances, there is more evidence of infection in acute bronchitis than in asthma, and dyspnea in acute bronchitis begins and ends gradually and paroxysms are absent. The physical signs, however, may be the same in both conditions. In children of allergic parents, acute bronchitis frequently precedes the development of asthma, or allergic bronchitis[11] may occur in which the diagnosis is extremely difficult to make. Chronic bronchitis in adults may be difficult to distinguish from asthma. The physical characteristics are the same, and the essential difference is the absence of paroxysms in chronic bronchitis.

Tracheobronchial stenosis is frequently mistaken for asthma. The obstructing lesion may arise within the lumen or may distort the passages by compression or traction from without. Dyspnea at first is present only on exertion; later it becomes constant with noisy respirations, and paroxysmal exacerbations of dyspnea occur. The dyspnea of tracheobronchial stenosis is both inspiratory and expiratory, although more marked during inspiration, and obstructive stridor is common. Stridor is not as marked or as harsh as in laryngeal stenosis and is greater in lesions near the larynx. Occasionally, stridor which has escaped notice may be demonstrated by asking the patient to breathe quietly with his mouth open, or by observing him during sleep. Cough is frequent and severe paroxysms may occur. Expectoration of blood occurs in most cases, usually in small amounts, and suggests the presence of an organic lesion.

On inspection of the thorax, the emphysematous changes, so common in asthma, are absent and the percussion note may be unaltered. The breath sounds are diminished below the site of the obstruction and if the obstruction is in one bronchus, it may be limited to that side of the thorax. In some cases there may be hyperresonance over the affected side.[8] Unilateral physical signs are of diagnostic significance, as in asthma both lungs are usually

equally involved. Bronchial spasm may be greater in one portion of the lung than in another in an occasional case of asthma, but the signs disappear with the subsidence of the attack.

Inflammatory strictures may result from tuberculosis or syphilis, or may be found above an area of bronchiectasis or a foreign body which has been in the lung for some time. Since bronchoscopy with dilatation of the stricture and removal of the foreign body, if present, will relieve the symptoms, the importance of a correct diagnosis is apparent. Vinson reported one case of extensive tuberculoma of the trachea, and one case of gumma of the bronchus is reported herewith. Adam, in 1926, reported four cases of tracheal tumor, in two of which the diagnosis of asthma had been made. Benign tumors of the bronchi are rare, but are more likely to be mistaken for asthma than malignant tumors, as the latter are rapidly progressive and the features of malignancy are usually prominent. Foreign bodies in the air passages may cause paroxysms of dyspnea and cough. Jackson described an asthmatoid wheeze which is heard in such cases.

Thymic asthma, resulting from compression of the trachea by an enlarged thymus gland, has been described frequently. Charles reported one case of paroxysmal asthma in which paroxysmal attacks were apparently due to hemorrhages into a large intrathoracic goiter, and relief from attacks followed thyroidectomy. I have observed several cases of intrathoracic goiter simulating asthma, and one of intrathoracic carcinoma of the thyroid gland with paroxysmal asthma-like attacks is reported herewith.

Calcified tracheobronchial lymph nodes may compress the bronchus and cause symptoms closely resembling asthma. Cameron, in 1915, stated that the condition may resemble asthma, and Wallgren, in 1925, reported three cases. Peshkin and Fineman, in 1926, reported three cases and reviewed the literature on the subject. They remarked that it was surprising to note how few references to the condition are found in American literature. Lapage and Adams cited the case of a child who obtained relief from asthmatic symptoms after coughing up several pieces of calcareous material.

Aneurysm of the aorta may often cause paroxysmal attacks of dyspnea, and other mediastinal tumors may occasionally give rise to asthma-like symptoms by compression of the air passages.

Hemoptysis, inspiratory dyspnea with stridor, constant dyspnea with or without paroxysmal exacerbations, and physical signs in one side of the thorax are important diagnostic points. Although the roentgen ray usually reveals the presence of mediastinal tumors, the roentgenograms may be negative in many cases of bronchial stenosis caused by intrinsic lesions. In many of these cases an accurate diagnosis can be made only by bronchoscopic examination.

The Lung.—Of the diseases of the lung which may simulate asthma, idiopathic pulmonary emphysema will offer the greatest difficulty in diagnosis. In many instances the diagnosis depends entirely on the presence or absence of a history of paroxysmal attacks. In emphysema, dyspnea is slowly progressive, and early in the disease is present only on exertion; as the disease progresses, wheezing and dyspnea follow the patient's slightest movement.

Pulmonary fibrosis due to pneumoconiosis, chronic fibrous tuberculosis, or to intensive roentgen-ray treatment in malignant lesions of the breast or mediastinum, may present symptoms which closely resemble asthma. In pneumoconiosis there usually is a history of long exposure to irritating dusts and, in cases of tuberculosis, other evidence of disease will be found on examination. Dyspnea occurring in any patient who has had roentgen-ray treatment over the thorax may be the result of pulmonary fibrosis. Roentgenograms of the thorax will reveal the characteristic changes in these conditions.

Occasionally, the onset of pneumonia or acute pneumonic tuberculosis may give rise to asthmatic symptoms, but the evidence of toxemia and the subsequent course of the disease soon make the diagnosis clear. Sudden pneumothorax may give rise to a severe paroxysm of dyspnea, but the characteristic features of asthma are absent and careful examination of the patient will reveal the true condition.

THE CIRCULATORY SYSTEM

Cardiac Asthma.—The use of the term "cardiac asthma" is probably responsible for much confusion in the diagnosis of asthma as it implies that the heart may be primarily at fault in certain cases. Although it is true that dyspnea is one of the most prominent symptoms of cardiac disease, most patients will have paroxysmal attacks only after exertion, and other evidence of myocardial failure will be apparent. There is an exception to this in the attacks of nocturnal dyspnea or smothering which occur in myocardial insufficiency, particularly of the left ventricle and often in association with coronary diseases. These attacks may rather closely resemble asthmatic paroxysms. They occur usually after the patient retires and may awaken him from sound sleep. There is a sense of oppression or heaviness in the thorax, and a feeling of suffocation with dyspnea and air-hunger. Respirations are usually more rapid than in asthma. A short hacking cough may be present and, in some cases, associated with pulmonary edema, pink frothy sputum may be expectorated. If pulmonary edema is present, moist râles will be heard; in many cases the breath sounds will be normal. The musical râles of asthma are usually absent and the patient appears to be in more distress and is more apprehensive than an asthmatic patient. Careful inquiry will usually reveal other evidence of the underlying condition, such as substernal pain or discomfort on exertion, dyspnea, on exertion, or slight pretibial and sacral edema. In some instances, it is impossible to distinguish one from the other without a period of observation and study. This is particularly true in elderly patients who, not infrequently, are subject to chronic bronchitis. Electrocardiographic studies may reveal changes characteristic of myocardial injury. Since the prognosis in asthma and myocardial failure is radically different, it is extremely important that a positive diagnosis be made and that the proper treatment be instituted.

Paroxysmal auricular flutter or fibrillation and, less commonly, paroxysmal tachycardia may be associated with dyspnea and pulmonary congestion. The symptoms at the onset of the attack, that is, the sudden palpitation, cardiac discomfort, and the un-

usual increase or irregularity in pulse rate do not occur with asthmatic paroxysms. The dyspnea of cardiac decompensation is accompanied by other signs of myocardial failure. Occasionally, bronchial asthma and cardiac disease may coexist. In these cases the cardiac disease may be a separate entity, or there may be gradual myocardial failure following the prolonged "overwork" of the myocardium occurring in severe asthma of long standing, particularly in patients having arterial hypertension. It is remarkable, however, how little cardiac injury is found at necropsy, even in patients who have had extremely severe asthma for many years.

A rather large number of patients, although they have typical asthmatic paroxysms, have been told that their symptoms are the result of cardiac disease. In this group the fear of death during paroxysms frequently produces a profound state of anxiety which is a considerable factor in increasing the frequency and severity of attacks. The assurance that the heart is not diseased and that death from cardiac failure in an asthmatic attack is a remote possibility, often affords great relief to these patients.

THE RENAL SYSTEM

The paroxysmal attacks of dyspnea which occur in primary renal disease and in renal insufficiency, the result of chronic hypertensive heart disease, are essentially the same as the attacks of dyspnea which occur in myocardial insufficiency.

THE NERVOUS SYSTEM

Disturbances of respiration are not uncommon in states of neurosis and of chronic nervous exhaustion. Occasionally, the diagnosis of asthma is made because of repeated attacks of dyspnea which are characterized by long, sighing respirations and a feeling that insufficient air is obtained by ordinary breathing. Usually the patient obtains relief after one long breath, but in some instances the condition may last for several minutes during which time he takes repeated deep sighing or yawning inspirations, and he may state that the air will not enter the lung

below a certain level. The attacks usually come on while the patient is resting and do not occur when his attention is diverted. Examination shows the lungs to be normal and the breathing disturbance is commonly but one of many complaints.

Hysterical dyspnea or polypnea is characterized by the rapid rate of respirations and the absence of dyspnea and cyanosis. The respiratory rate may be high, 100 a minute in the case reported herewith, whereas the respirations in asthma are slow and labored. Examination of the lungs reveals none of the signs of asthma, and other stigma of hysteria may be present.

Respiratory disturbance following encephalitis[6, 9] is responsible for paroxysmal attacks of noisy breathing; occasionally it may be confused with asthma. It occurs most often in children and occasionally in adults. In children there often is an associated change in personality and behavior. The respiratory symptoms consist of a series of deep noisy respirations followed by a period of apnea during which the patient stretches and goes through a series of stereotyped actions. True dyspnea and the characteristic pulmonary signs of asthma are absent, and the history of encephalitis preceding the respiratory symptoms can be obtained in most cases.

ABSTRACTS OF CASES

Case 1.—A man, aged forty-two years, complained of shortness of breath of nine months' duration. For four months paroxysms of cough and dyspnea accompanied by audible stridor had occurred at night and he had been unable to sleep lying down. He had not obtained relief from asthma remedies. His voice had been husky for four years and especially so for the last two and a half months. He also complained of occasional lightning pains in the legs. Definite inspiratory stridor and dyspnea were noted on examination, and a few musical râles were heard in the thorax. Argyll-Robertson pupils were present, and the patellar reflexes were absent. The vocal cords were fixed in median-line position. The Wassermann reactions of the blood and spinal fluid were positive. Tracheotomy became necessary, and intensive antisyphilitic treatment was instituted. Examination a

year later showed that the cords were still paralyzed. A chrondroma of the larynx was found and removed.

Case 2.—A woman, aged sixty-four years, complained of increasing dyspnea for eight months, which gradually became constant with cough and expectoration. For four months she had had paroxysmal attacks of severe dyspnea which the usual treatment for asthma had not relieved. She had lost 30 pounds in four months. Definite obstructive stridor was present and, although the thyroid gland was not palpable, examination revealed upper mediastinal widening, and roentgenograms of the thorax disclosed a large intrathoracic goiter. At operation a papillary adenocarcinoma of the thyroid gland was removed with relief from symptoms.

Case 3.—A woman, aged fifty-one years, was referred for treatment of asthma which had been present for two years. She complained of paroxysmal nocturnal attacks of cough and wheezing. Marked dyspnea on exertion had been present for several months. Medicine for asthma afforded some relief. Examination revealed inspiratory and expiratory dyspnea and a harsh cough. Breath sounds were absent over the left upper lobe and much diminished over the left base. Roentgenograms of the thorax were negative. The Wassermann reaction of the blood was strongly positive. Bronchoscopy revealed a lesion at the bifurcation of the trachea, with almost complete obstruction of the left bronchus. After two weeks of antisyphilitic treatment, marked improvement was noted and the diagnosis of probable gumma of the bronchus was made.

Case 4.—A man, aged forty-one years, had had hemoptysis on two or three occasions four years before coming to the clinic, and tuberculosis had been diagnosed. Two years later following pneumonia, paroxysms of cough and wheezing occurred every morning as he got out of bed. Epinephrine gave some relief. He had noticed constant, moderate dyspnea for about a year. On examination high-pitched inspiratory and expiratory stridor

and physical signs of partial obstruction of the right main bronchus were found. Musical râles were present. Roentgenograms of the thorax showed pleural thickening in the base of the left lung, and there was a history of pleurisy on the left side sixteen years previously. At bronchoscopy the right bronchus was found to be almost completely obstructed by a tumor at the bifurcation. For the last five years repeated treatments with surgical diathermy have given symptomatic relief. Following one treatment, several hairs were coughed up in addition to necrotic tumor tissue, and a diagnosis of dermoid cyst of the bronchus was made.

Case 5.—A woman, aged forty-two years, had had typical asthmatic attacks since childhood. Roentgenograms of the thorax showed a circumscribed nodule in the upper right mediastinum resembling an aneurysm. Bronchoscopy revealed an ulcerating mass in the right bronchus and tissue removed was found to be adenocarcinoma. Death occurred a year later. In this case, a primary tumor of the bronchus of an asthmatic patient was discovered by roentgen ray and confirmed by bronchoscopy.

Case 6.—A man, aged fifty-two years, complained of asthmatic attacks of four months' duration. The attacks were nocturnal and associated with cough. He also had some dysphagia at times. The pupillary reflexes were sluggish and there was extensive leukoplakia of the tongue and cheek. The left vocal cord was fixed. Inspiratory and expiratory dyspnea were present, and were increased when the patient was lying down. Mediastinal dulness was increased and a tracheal tug was present. Musical râles were heard over both lungs. Fluoroscopic examination revealed an aneurysm of the aorta. The Wassermann reaction of the blood was strongly positive.

Case 7.—A man, aged forty-three years, had been treated for tuberculosis in 1917. Following influenza in 1927 paroxysmal attacks of dyspnea developed which gradually increased on ex-

ertion. Bacilli of tuberculosis were found in the sputum. Sanatorium treatment had improved the general condition, but the asthma had become worse and he had been unable to lie down at night. Examination revealed evidence of almost complete obstruction of the left main bronchus. Roentgenograms showed extensive fibrosis of both upper lobes and at bronchoscopy the left main bronchus was found to be almost completely obstructed by pressure from below and the right bronchus was found to be obstructed to a lesser degree. A diagnosis of tuberculous tracheobronchial nodes was made.

Case 8.—A man, aged fifty-one years, complained of dyspnea and wheezing on exertion for the last four years with recent nocturnal attacks. He also had had paroxysms of cough with expectoration of purulent sputum. Recently, skin tests had shown positive reactions to several foods. The thorax was emphysematous and roentgenograms showed bilateral fibrosis of the middle portion of both lungs. Further inquiry revealed that between the ages of sixteen and twenty-five he had worked in quartz mines, and a diagnosis of pneumoconiosis was made.

Case 9.—A man, aged seventy-one years, in the last three weeks had had three nocturnal attacks of dyspnea, cough, and a choking sensation in the thorax associated with "chest noises" which were audible at some distance. Precordial distress following exertion had been noticed for six weeks. The systolic blood pressure was 184, and the diastolic 90, the heart was moderately enlarged, and the electrocardiogram showed significant changes. A diagnosis of coronary sclerosis was made. Sudden death occurred five months later.

Case 10.—An unmarried woman, aged twenty-three years, complained of attacks of nocturnal dyspnea which she had had since the age of fifteen. Between the ages of eighteen and twenty-one she had been free from attacks. The attacks occurred from six to eighteen times a year and usually lasted until morphine was given. Some attacks were associated with wheezing and

others were not. The attacks came on suddenly with a terrific tightening in the throat and often the patient was unable to talk. During attacks the respiratory rate was much increased, reaching 100 in one attack. Expiration was short and produced by a sudden contraction of the muscles of the thorax with a contraction of the abdominal muscles, causing the patient to bend forward with each breath. At times she actually bounced up and down in bed with each breath. During one attack which lasted for twenty-four hours, she would doze for a few minutes, during which time the breathing was normal. Musical râles were heard with one attack occurring in the presence of an acute cold, but they were absent in other attacks. Examination, including a complete neurologic examination, was negative. Fluoroscopic examination during an attack showed nothing abnormal. A diagnosis of hysteria was made.

SUMMARY

The outstanding characteristics of asthma have been considered and an outline is presented of conditions which may cause dyspnea resembling asthma. Case reports illustrate a few of the conditions.

It is extremely difficult to make a diagnosis in certain conditions that may cause dyspnea which closely resembles asthma. Other conditions with only a superficial resemblance may be mistaken for asthma, and the importance of a carefully taken history and complete examination before making the diagnosis is emphasized.

In some cases an accurate diagnosis can be made only after bronchoscopy.

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BLEEDING DUODENAL ULCER WITH PERFORATION AND OBSTRUCTION; COMPLICATIONS IN THE PREOPERATIVE MANAGEMENT

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THE following case is reported because of the significant complications which occurred and because of the etiologic and therapeutic problems which arose.

A man, aged sixty years, came to the clinic October 17, 1929, complaining of gastric trouble of long duration. There was nothing in the past history or in the family history of significance except that one of his four children was convalescing from recently acquired pulmonary tuberculosis. He had had yearly attacks of intermittent dyspepsia for thirty years. The attacks had usually been most noticeable in July and August, and had been characterized by a dull gnawing epigastric pain occurring about three or four hours after meals and relieved by rest, food, or soda. During this period he had occasionally been awakened at night by the same type of distress. He had vomited rarely until September, 1929, but since then had vomited frequently, and recently, on several occasions, had vomited fairly large quantities of food, some of which had been eaten the preceding day. The pain also had been more severe and more difficult to control than with previous attacks. However, he had been on an exclusive milk diet since September 10, with some relief. During this time he had tried to take about 60 c.c. of milk every hour when awake, but had frequently been unable to do so because of anorexia. He had not taken alkalies. He had been unable to work since September 10, because of pain and frequent vomiting and since then he had lost 17 pounds in weight. On the day before admission he had noticed slight melena for the first time.

Examination at the clinic showed that the patient was moderately dehydrated. He did not appear anemic or cachectic. Aside from definite tenderness in the epigastrium, the results of general examination were essentially negative for a man of his age. The temperature and pulse rate were normal. The systolic blood pressure was 130, and the diastolic 90. Urinalysis was negative. The Wassermann reaction of the blood was negative. The hemoglobin (Dare) was 78 per cent; erythrocytes numbered 4,080,000, and leukocytes 10,700. The blood urea was 74 mg. for each 100 c.c. The carbon dioxide combining power of the plasma was 93 volumes per cent, and the plasma sodium chloride was 479 mg. for each 100 c.c. A roentgenogram of the thorax showed a healed tuberculous lesion of the upper part of the right lung.

A tentative diagnosis of bleeding peptic ulcer with obstruction and probably chronic perforation was made, and the patient was sent immediately to the hospital for preoperative treatment. A light liquid diet was prescribed and a solution of 10 per cent glucose and 1 per cent sodium chloride was given intravenously in an attempt to overcome the toxemia associated with the duodenal obstruction. From 1 to 2 liters of this solution was given intravenously each day (Fig. 167).

Moderate melena continued and on the fifth day after admission to the hospital the patient fainted as the result of a severe gastro-intestinal hemorrhage. Following this, he passed several black liquid stools. The hemoglobin and erythrocytes dropped rapidly until October 24, 1929 (six days after admission), when the hemoglobin was 25 per cent (Dare) and erythrocytes numbered 1,440,000. A transfusion of 500 c.c. of citrated blood was given and this was repeated the next day and again five days later. Under this regimen there was definite improvement. The gastro-intestinal bleeding was controlled, and the blood count began to improve. The toxemia resulting from obstruction of the upper intestinal tract was corrected (Fig. 167), and the patient felt and looked stronger.

At this time, however, slight edema of the feet and ankles was noted, and so it seemed advisable to diminish the intake of

fluid and sodium chloride. The intravenous injections were discontinued, but nevertheless the edema spread rapidly over the body until four days later the patient had moderate anasarca, which was especially striking in the dependent parts of the body. There was no apparent cardiac basis for this edema and it seemed

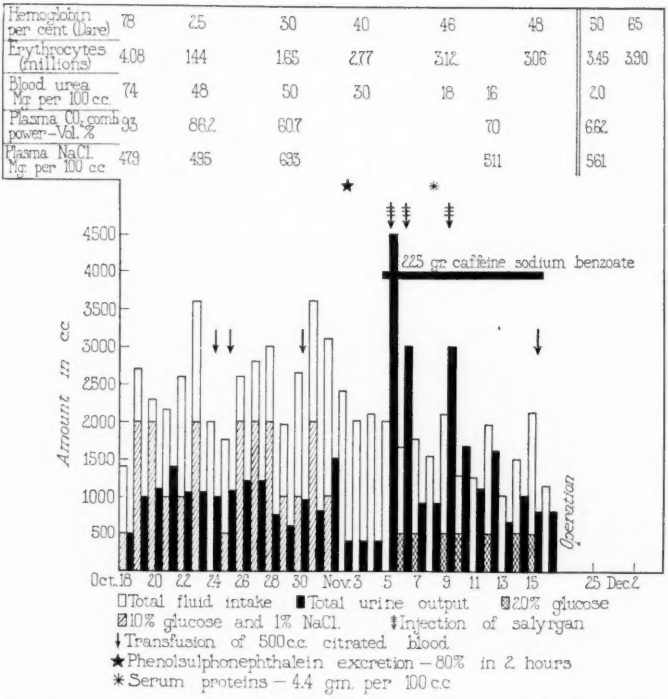
Hemoglobin per cent (Dare) 78 25 30 40 46 48 50 65
Erythrocytes (millions) 4.08 144 165 277 312 306 3.45 3.90
Blood urea Mg. per 100 cc. 74 48 50 30 18 16 2.0
Plasma CO2 comb. power—Vol. % 93 86.2 60.7 70 66.2
Plasma NaCl. Mg. per 100 cc 479 495 635 511 561
4500
4000
3500
3000
2500
2000
1500
1000
500
Amount in cc
2.25 gr caffeine sodium benzoate
Operation
Oct. 18 20 22 24 26 28 30 Nov. 3 5 7 9 11 13 15 25 Dec. 2
Total fluid intake
Total urine output
20% glucose
10% glucose and 1% NaCl.
Injection of salyrgan
Transfusion of 500 cc. citrated blood.
Phenolsulphonephthalein excretion — 80% in 2 hours
Serum proteins — 4.4 gm. per 100 cc

Fig. 167.—Laboratory data in complicated case of bleeding duodenal ulcer with obstruction.

to be the result of high intake of fluid and sodium chloride in a patient whose serum proteins had been lowered by insufficient diet and by hemorrhage, and in whom mild toxic nephrosis probably existed as a result of the high intestinal obstruction.

The patient was then given 20 per cent solution of glucose intravenously, in smaller quantities (Fig. 167). The total intake

of fluid was also diminished somewhat but a diet higher in protein was prescribed. Caffeine sodium benzoate was given hypodermically in doses of 7.5 grains three times a day as a diuretic, and three injections of salyrgan were given intravenously in doses of 0.5, 1.0, and 0.75 c.c., respectively (Fig. 167). These therapeutic measures resulted in prompt and striking diuresis. Following the first injection of salyrgan, the output of urine was 4,500 c.c. in twenty-four hours and following the second and third injections it was 3,000 c.c. in twenty-four hours. The edema disappeared rapidly, the hemoglobin rose to 48 per cent (Dare) and the erythrocytes to 3,060,000, and the patient felt much stronger. The blood urea in the meantime had remained at 16 mg. for each 100 c.c., and the carbon dioxide combining power of the plasma at 70 volumes per cent, but the plasma sodium chloride had dropped to 511 mg. for each 100 c.c. It seemed as if surgical procedures were now advisable. Therefore, another transfusion of 500 c.c. of citrated blood was given and the operation was performed, November 18. An ulcer was found on the posterior wall of the duodenum about 2.5 cm. from the pylorus. It had a crater about 2 cm. in diameter which had perforated onto the pancreas, producing pancreatitis and obstruction. Posterior gastro-enterostomy was performed and the patient made a good recovery. Slight edema of the ankles was noted postoperatively, but this was easily controlled by restriction of sodium chloride and moderate restriction of fluid.

One week after operation the blood urea, the carbon dioxide combining power of the plasma, and the plasma chlorides were ali normal; the hemoglobin was 50 per cent (Dare) and the erythrocytes numbered 3,450,000 (Fig. 167). A week later the hemoglobin was 65 per cent (Dare) and the erythrocytes numbered 3,900,000. The patient was dismissed December 11 in good general condition and with the wound healed.

COMMENT

The history in this case is typical of long-standing peptic ulcer with more recent perforation, obstruction, and hemorrhage. The chemical changes in the blood are characteristic of those

seen in cases of high intestinal obstruction wherein the blood urea is elevated, the carbon dioxide combining power of the plasma is increased, and the chlorides are diminished.

The usual correction of the toxemia is by the intravenous injection of 10 per cent glucose and 1 per cent sodium chloride.[3] In some cases this is supplemented by gastric lavages, but in this case because of the hemorrhages and because the vomiting was easily controlled this was not deemed advisable. The case illustrates the syncope and melena resulting from bleeding duodenal ulcer, shows the degree of anemia that may result, and the value of transfusions of blood in controlling the bleeding and correcting the anemia. The occurrence of the marked edema during treatment brings up another problem. It seemed probable that the patient's serum proteins were low, with a corresponding decrease in the serum osmotic pressure because he had not taken sufficient protein or sufficient food for nearly two months and because he had had a severe intestinal hemorrhage. This impression was confirmed when the serum proteins were found to be 4.4 gm. for each 100 c.c. even after three transfusions of 500 c.c. of blood in each had been given. There was probably a mild degree of acute toxic nephrosis, as suggested by the trace of albumin in the urine, by the elevated blood urea on admission, and by mild albuminuria later. This was never a prominent factor, however, inasmuch as most of the time the urinalysis was negative and at the time of the onset of edema the blood urea was 30 mg. for each 100 c.c. and the excretion of phenolsulphonephthalein was 80 per cent in two hours. The rather liberal intake of salt and fluid also would tend toward the production of edema and yet rarely does edema occur in cases of upper intestinal obstruction wherein similar amounts of salt and fluid have been given. It seems probable that the edema was due to a rather liberal intake of salt and fluid in the presence of a tendency toward edema because of the lowered serum proteins[2] and the mild toxic nephrosis, the extrarenal factors playing by far the major part. In attempting to eliminate the edema, restriction of fluid and salt seemed of primary importance. For this reason the intravenous injection of 1,000 to 2,000 c.c. of 10 per cent

glucose and 1 per cent salt daily was discontinued and instead 500 c.c. of 20 per cent glucose without salt was given intravenously daily. The three transfusions of blood helped to raise the serum proteins, and the proteins in the diet were raised as much as possible for the same reason.

In spite of these therapeutic measures, the edema was resistant to treatment and so the use of suitable diuretics seemed advisable. The alkaline diuretics were contra-indicated because of the recent alkalosis, and the acid-producing salts, such as ammonium nitrate, ammonium chloride, or calcium chloride, were not used because of the fact that the patient was easily nauseated, and it seemed unlikely that he would tolerate them. Therefore he was given a purine diuretic, in the form of caffeine sodium benzoate, subcutaneously. In order to obtain further diuresis he was given small doses of salyrgan intravenously. There seemed to be no contra-indications to this drug, inasmuch as there was no evidence of true nephritis and the edema was mostly due to extrarenal factors. Following a small dose of 0.5 c.c. intravenously, the diuretic response was so marked that there seemed no need of large doses. Two small doses were given subsequently, with good diuresis each time, again illustrating the efficacy of repeated small or moderate doses of salyrgan in suitable cases, especially when combined with other diuretics.[1] The drop in the blood chlorides in this case following the injections of salyrgan was probably due to the saline diuresis. The rapid recovery following gastro-enterostomy was noteworthy.

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SOME MEDICAL ASPECTS OF PROSTATIC OBSTRUCTION

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RECENT studies have added to our knowledge of the underlying physiologic and chemical changes associated with obstructive lesions of the urinary and biliary tracts as well as of the stomach and bowel. The recognition and treatment of such changes have made it possible to institute preoperative preparation and anticipate postoperative complications, thereby reducing the mortality and bringing about better final results.

At the clinic 95 per cent of the patients who present themselves with prostatic obstruction are aged more than fifty years, and 75 per cent are between the ages of sixty and seventy-five years. It would seem logical to find in this group of patients degenerative diseases of the cardiovascular and renal systems which are the results of age and disease. Furthermore, it would be expected that from the point of time alone the chances of the development of malignant disease, hyperthyroidism, and diabetes would increase with each succeeding year of life. This supposition, so far as the cardiovascular systems are concerned, has been corroborated by Willius who, in the observation of 705 patients with prostatic obstruction, found cardiovascular disease in 42 per cent. The diagnosis and relief of prostatic obstruction is largely a problem for the urologist and urologic surgeon. However, it becomes the duty of the internist to determine the general condition of the patient so far as he may have other complicating ailments, in order to evaluate the condition of the cardiovascular and renal systems. Such a study often reveals defects in which preoperative treatment will lower the risk of surgical procedures and aid in the selection of cases and in the type of operation.

It is extremely important in every case of prostatic obstruction to secure a detailed history, and to make a thorough general examination. Special examinations and laboratory studies should be carried out as the case warrants. The following reports indicate some of the problems arising in cases of prostatic obstruction.

REPORT OF CASES

Case 1.—A man, aged sixty-six years, came to the clinic April 16, 1929. He had been told that he had carcinoma of the intestines. The family history and his past history were not significant. The patient stated that he had noted, for two months, a gradually enlarging growth in the lower part of the abdomen. He had lost a little weight, and frequently had an uncomfortable full feeling in the abdomen after meals. Constipation had been progressive. There were no other symptoms referable to the gastro-intestinal tract. For a year he had experienced increasing difficulty in starting the urine and there was urinary frequency and nocturia every one to two hours. He passed only small amounts of urine and occasionally was incontinent. He felt that the bladder was never completely emptied. Hematuria had not been noted.

Examination showed moderate loss of weight, dry skin, pallor, and a dry reddened tongue. There was a moderate degree of generalized arteriosclerosis. The pupils were equal and reacted normally to light and accommodation. The heart was slightly enlarged, but the tones were regular and of good quality, and murmurs were not heard. The systolic blood pressure was 190 and the diastolic 100; the pulse was 86, and the temperature 97° F. The lungs were normal. In the abdomen was a symmetric smooth cystic globular mass extending from the symphysis pubis well above the umbilicus. The external genitalia were normal. Rectal examination revealed enlargement of the prostate gland, graded 3. Other rectal abnormality was not found. The reflexes were normal.

A diagnosis was made of hypertrophy of the prostate gland, with overdistention of the bladder. The patient was immediately hospitalized, and gradual decompression of the bladder was

started. The urine showed albumin, graded 3, and a few erythrocytes, but no pus cells. The hemoglobin was 65 per cent (Dare); erythrocytes numbered 3,840,000, and leukocytes 9,000. The blood urea was 72 mg. for each 100 c.c. After thirty-six hours the decompression apparatus was removed, and an indwelling urethral catheter was left in place. A phenolsulphonephthalein test was made; collection at thirty-minute intervals over a two-hour period showed a faint trace of the dye at the end of thirty minutes, 5 per cent at two succeeding periods, and only a faint trace in the last period, a total of 10+ per cent. Five hundred cubic centimeters of physiologic solution of sodium chloride were given intravenously each day until the blood urea approached normal limits. The total daily intake of fluid averaged 4,000 c.c., and the ratio between intake and output was satisfactory. A diet containing about 40 gm. of protein in twenty-four hours was prescribed, and, as the patient was not acutely ill, he was urged to be out of bed most of the day. Under this regimen the blood urea dropped gradually from 72 to 24 mg. for each 100 c.c. in fourteen days. The phenolsulphonephthalein test then showed a return of 20 per cent, 15 per cent, 5 per cent, and a faint trace, a total of 40 per cent, in successive thirty-minute periods. In the meantime roentgenograms did not reveal evidence of malignancy in the stomach or colon. The Wassermann reaction of the blood was negative. Electrocardiograms did not reveal abnormality. May 7, 1929, suprapubic prostatectomy was done. There were no postoperative complications, and the patient had an uneventful convalescence.

Case 2.—A man, aged sixty-six years, came to the clinic, September 29, 1928. He was admitted to the hospital as an emergency case, because he was unable to void urine. He stated that during the ten years previous to his coming he had noted increasing urinary frequency, nocturia, and slowness in starting the urinary stream. Six days before admission he had had acute urinary retention and had been catheterized twice daily since that time. There were no symptoms of importance referable to the gastro-intestinal tract, heart, or lungs.

The pupils reacted normally to light and accommodation. The heart was moderately enlarged. There was generalized peripheral arteriosclerosis, graded 3. The systolic blood pressure was 230, and the diastolic 140. The bladder was distended and reached the level of the umbilicus. The prostate gland was enlarged, graded 3, and was smooth, firm, and symmetric. It was considered to be benign. Gradual decompression of the bladder was started. The urine contained a trace of albumin and numerous pus cells. The hemoglobin was 72 per cent (Dare); erythrocytes numbered 4,720,000, and leukocytes 9,100. The blood urea was 68 mg. for each 100 c.c. The Wassermann reaction of the blood was negative. Roentgenograms of the thorax, kidneys, ureters, and bladder were negative. The electrocardiogram did not show significant changes. A cystogram revealed a normal outline of the bladder, with some sacculation of the dome. A diagnosis of prostatic hypertrophy with urinary obstruction and secondary renal insufficiency was made. In order to improve the renal function, a permanent indwelling urethral catheter was kept in place after the decompression apparatus had been removed. The intake of fluid was maintained at 3,000 to 4,000 c.c. with daily intravenous injections of 1,000 c.c. of physiologic solution of sodium chloride. Hot packs were applied occasionally. During the twenty-one days of treatment the blood urea varied between 68 and 40 mg. for each 100 c.c., and the blood pressure did not go below 164 and 114.

Because of renal insufficiency, two-stage suprapubic cystostomy was performed. After three weeks the patient was allowed to return home for a few months, after which time he was advised to return for consideration of prostatectomy. It is worthy of note that following such a comparatively simple procedure as cystostomy, the blood urea rose to 90 mg. for each 100 c.c.

The patient returned March 20, 1929, at which time his general condition had improved remarkably. The blood urea was 36 mg. for each 100 c.c. The blood pressure was 180 and 100, and 170 and 90, on successive days. The output of phenolsulphonephthalein was 20 per cent, 15 per cent, 10 per cent,

and 5 per cent, a total of 50 per cent, in successive thirty-minute periods. After a few days' observation prostatectomy was performed. The patient had a normal convalescence, and was dismissed from observation the nineteenth day after operation.

These two cases illustrate some of the problems encountered in acute urinary obstruction secondary to prostatic hypertrophy. An acutely distended bladder is frequently overlooked and if it is discovered it is often mistaken for some other type of abdominal tumor. The bladder may be greatly enlarged in certain cases with almost no urinary symptoms. A patient was recently observed who, for two years, had had an abdominal tumor extending from the symphysis to the umbilicus. The tumor was found to be a distended bladder, but there were no urinary symptoms except occasional nocturia and slight incontinence. The danger of sudden emptying of an overdistended bladder has been frequently pointed out. Following this procedure, fall in blood pressure, hemorrhage, edema, and hyperemia of the urinary tract may be followed by anuria and uremia. If the bladder contains residual urine of more than 150 c.c., gradual decompression should be instituted.

The determination of renal function and its improvement if possible in cases of renal insufficiency is one of the most important single considerations in the care of patients with urinary obstruction, and has direct bearing on the outcome of surgical procedures on the prostate gland. As a result of infection of the bladder, which invariably sooner or later accompanies prostatic hypertrophy and residual urine, secondary pyelonephritis develops, and, as the result of the back-pressure of an overdistended bladder, renal tubular degeneration develops, all of which lowers the functional capacity and reserve of the kidney. The patient in such a case is weak and exhausted by loss of sleep due to urinary frequency and a failing appetite. The presence of nausea and vomiting may indicate uremia. In such a case a diagnosis of gastric malignancy is common. The patient has learned that the more fluid he takes the more frequently he urinates; therefore, he takes less fluid, and dehydration results, as shown by

dry inelastic skin. The eyes lose their luster, the tongue is dry, red, and coated, the breath has the odor of urine, and the pulse is weak and thready. Such a patient is uremic and bordering on cardiac failure.

The first consideration is the establishment of drainage of the bladder. This is best accomplished by first gradually decompressing the bladder and then continuing drainage by the use of the permanent urethral catheter. The next important step is the intake of fluids. A daily intake of 3,000 to 4,000 c.c. should be maintained. If it is impossible for the patient to take this amount by mouth, physiologic solution of sodium chloride should be given intravenously; it may be given in amounts varying between 500 and 1,000 c.c. twice daily. The sodium chloride solution can be given practically without danger if it is properly prepared and given slowly. Fluids given in this manner cause much less discomfort to the patient than subcutaneous infusions or proctoclysis.

In tests of renal function, the estimation of the blood urea and the excretion of phenolsulphonephthalein is relied on almost entirely. The normal value for blood urea varies between 18 and 40 mg. for each 100 c.c. It has been shown, however, by Frontz and Geraghty that these figures are subject to considerable variation, and blood urea of 50 mg. cannot be considered as abnormal in persons on a high-protein diet. Furthermore, these authors have observed patients with definite renal impairment on a moderate protein diet whose blood urea ranged between 60 and 80 mg., and who, on restriction of protein, promptly had a drop in blood urea below the upper limit of normal. It has been observed frequently that reduction in the amount of blood urea follows the intake of large quantities of water.

It is important, therefore, that in the estimation of renal function the nitrogenous elements in the diet, as well as the intake of fluid, be taken into consideration. In the clinic patients with prostatic obstruction are placed on a diet containing about 40 gm. of protein a day, and they are urged to take about 3,000 c.c. of fluid in twenty-four hours. This gives a standard basis for comparison.

The estimation of blood urea is not a test of the excretory capacity of the kidneys, but merely a means of determining the degree of retention of a substance normally eliminated. The excretory capacity is best determined by means of the phenolsulphonephthalein test; an output of between 50 and 70 per cent in two hours is usually considered normal. Braasch and Kendall have shown the value of the intravenous injection of phenolsulphonephthalein over the intramuscular injection; they found a difference as high as 20 per cent in the same person. The studies of Shaw in determining an elimination curve of phenolsulphonephthalein in normal and abnormal conditions have added distinct value to the test. Shaw suggested the collection of the urine at fifteen-minute intervals for two hours after the intravenous injection of 6 mg. of the dye dissolved in 1 c.c. of distilled sterile water. It was found that the normal curve was characterized by an average output of 40 per cent during the first fifteen-minute period, 17 per cent during the second, 8 per cent during the third, 4 per cent during the fourth, and a gradual decrease to 0.5 per cent during the eighth.

Many of Shaw's cases were cases of renal insufficiency due to infection and back-pressure from prostatic obstruction. In all cases of known renal disease, there were definite abnormalities in the curve of excretion. It was found, furthermore, that with the improvement in renal function the peak of elimination appeared earlier, whereas the total amount excreted in the two-hour period remained the same. These observations have been corroborated in the clinic on numerous occasions. If the test is applied to patients wearing an indwelling urethral catheter, the collection of the urine at fifteen-minute intervals is quite simple; however, if such a catheter is not inserted, some patients have difficulty in voiding as often as every fifteen minutes. Bugbee's suggestion of collecting the urine at thirty-minute intervals has been followed with satisfactory results.

The majority of patients with prostatic obstruction will be found to have a fair degree of renal function as determined by clinical and laboratory observations. Renal insufficiency is frequently seen in two types of patients: Those in whom symptoms

have been of short duration with the sudden development of acute retention, and those in whom symptoms of a moderate degree have been present for a long period and who may or may not be suffering from acute retention. The blood urea may be found to be as high as 100 mg. or even 200 mg. for each 100 c.c., and the output of phenolsulphonephthalein as low as 10 per cent, with a definitely abnormal curve for the excretion of phenolsulphonephthalein. In patients whose symptoms have been of short duration, and acute retention has developed, the institution of gradual decompression followed by continuous drainage of the bladder frequently results in rapid recovery of renal function. On the other hand, patients who have had obstruction to the neck of the bladder for years are more likely to experience varying degrees of permanent renal injury. Continuous drainage of the bladder is one of the most important aids in cases of renal insufficiency secondary to prostatic obstruction. It has been the experience in the clinic that the intravenous injection of fluid is more effective in improving renal function than the intake of an equal quantity of fluid by mouth, although the latter should not be neglected. Not more than 500 c.c. should be given at one time to patients with myocardial weakness. One or two hot packs may be given daily, depending on the general condition of the patient and how well the packs are tolerated. Mild saline cathartics should be given to aid elimination by the bowel. If there are no contra-indications, the patient should be urged to be out of bed at least part of the day and to walk in the corridors; in warm weather he should be out of doors. He must wear sufficient clothing so as not to become chilled. Edema is rarely seen in renal insufficiency associated with prostatic obstruction so that diuretics such as ammonium chloride, salyrgan, and merbaphen are of no help and may actually be harmful. At times a mild degree of edema is seen in patients who are under preparation for operation, and it will usually be found that in their eagerness to carry out the physician's advice to drink large quantities of water, they have overdone it, taking as much as 5 to 7 liters a day. Reducing the intake of fluid is usually all that is required to eliminate the edema.

At other times, during acute pyelonephritis which may arise during preoperative preparation or more commonly immediately after prostatectomy, a rather marked discrepancy between intake and output of fluid will be noted. If the intake of fluid is pushed and especially if the intravenous injections are continued, a moderate amount of edema may appear. Under such circumstances it is frequently advisable to discontinue intravenous injections of solutions of sodium chloride and substitute 10 per cent glucose. Caffeine diuretics may help and should be given in fairly large doses. Mercurial diuretics, except in selected cases, are contraindicated. Occasionally the use of 10 c.c. of a 1 per cent solution of mercurochrome or gentian violet intravenously has given striking results in acute pyelonephritis.

In some cases it may be noted that following temporary improvement in renal function, as evidenced by clinical observation and estimations of blood urea, and of the excretion of phenolsulphonephthalein, the renal condition seems to reach a level and remain there. This may at times be taken as an index of the amount of permanent renal injury. Many such patients, however, have been subjected to cystostomy and the patients returned in three or four months, improved not only as regards the renal function, but generally, and able to withstand prostatectomy without difficulty. This is well illustrated in Case 2. Kidneys affected with pyelonephritis secondary to prostatic obstruction have remarkable recuperative powers. With the institution of drainage of the bladder, and the resulting relief of infection and back-pressure, it is probable that edema in the parenchyma of the kidney is diminished and circulation improves with improvement in renal function. It is often observed at necropsy that only a small amount of functioning renal tissue remains, and yet there was no demonstrable evidence of renal insufficiency during life. Such a kidney will carry on its function satisfactorily if complications do not arise, but in the presence of postoperative hemorrhage or recurrent pyelonephritis there is not enough reserve to maintain life. The length of time during which prostatic obstruction has been present or the history of

repeated attacks of pyelonephritis may lead one to suspect such a situation.

Case 3.—A man, aged sixty-nine years, came to the clinic June 7, 1929, complaining of trouble with the bladder and prostate gland of six years' duration. The patient's father had died of pulmonary tuberculosis. During the last six years the patient had noted a progressive increase in urinary frequency and nocturia. On nine occasions during this time he had had acute urinary obstruction and had had to be catheterized; once he had had gross hematuria. In the two months preceding his admission he passed small amounts of urine every one to two hours. There were no symptoms referable to the gastro-intestinal, respiratory, or cardiovascular systems.

The patient appeared to be well developed and well nourished, and was well preserved for his age. The systolic blood pressure was 130, and the diastolic 80. There was a moderate amount of arteriosclerosis of the peripheral vessels. The heart was not enlarged, but the tones were of poor quality and distant. The heart beat was 70 a minute and regular, and there were no murmurs. Examination of the lungs and abdomen did not reveal abnormalities. The prostate gland was enlarged, graded 2. The urine contained numerous erythrocytes and pus cells; albumin was graded 3. The blood urea was 24 mg. for each 100 c.c. The phenolsulphonephthalein test showed a return of a faint trace, 35 per cent, 5 per cent, and a faint trace of the dye in successive thirty-minute periods. The hemoglobin was 80 per cent (Dare); erythrocytes numbered 4,320,000, and the leukocytes 9,200. Roentgenograms of the kidneys, ureters, and bladder revealed multiple shadows in the region of the bladder. There was about 120 c.c. of residual urine. A cystogram showed the outline of a normal-sized bladder with trabeculation and marked elevation, and filling defect in the region of the prostate gland. There were multiple shadows over the prostatic area suggestive of stones in the prostate gland. A diagnosis of marked prostatic hypertrophy and prostatic stones was made. Prostatectomy was advised. The patient was prepared for operation

by inserting a permanent indwelling urethral catheter for ten days. The electrocardiogram revealed a heart rate of 89, sinus rhythm, inverted T wave in derivations I, II, and III, and incomplete bundle-branch block, and QRS widths of 0.14 second.

Suprapubic prostatectomy was performed June 17, 1929. The pulse rate rose to 122 following the operation, but in forty-eight hours had returned to 80 and varied after that between 70 and 90. The postoperative convalescence was uneventful and the patient was dismissed from observation on the twenty-fourth day after operation.

Case 4.—A man, aged fifty-nine years, came to the clinic February 2, 1929, complaining of trouble in the bladder which he had had for a year. His father had died at the age of seventy-five years of Bright's disease, and his mother was well at the age of eighty-three. The patient had had influenza three times and pneumonia at the age of twenty years. For a year the patient had had urinary frequency and nocturia, with increasing difficulty in starting the urine; the stream was small and there was some dribbling. He had been catheterized on several occasions on account of acute retention. Following the catheterization he had had fever and chills, hematuria, and the testes were swollen and tender for ten days. For two weeks there had been constant pain in the perineum. He had lost gradually in strength and weight. There were no symptoms referable to the cardiovascular, respiratory, or gastro-intestinal systems.

The patient weighed 178.5 pounds; his usual weight was 190 pounds. The systolic blood pressure was 110, and the diastolic 80. The heart and lungs were objectively normal. The bladder was slightly distended. The left testis was swollen, reddened, and tender. The prostate gland was enlarged, graded 3, and rather hard and irregular, but was considered to be benign. The urine contained a trace of albumin and numerous pus cells and erythrocytes. The hemoglobin was 61 per cent (Dare); erythrocytes numbered 4,080,000, and the leukocytes 5,600. The blood urea was 26 mg. for each 100 c.c. and the phenolsulphone-

phthalein test showed a return of 25 per cent, 30 per cent, 10 per cent, and a faint trace in successive thirty-minute intervals. A roentgenogram of the thorax was negative, and that of the kidneys, ureters, and bladder did not show urinary calculi. The electrocardiographic tracing did not reveal anything of significance. Following urethroscopic and cystographic studies, a diagnosis of prostatic hypertrophy was made, and operation advised. The patient was hospitalized, a permanent indwelling urethral catheter was inserted, and further preparations for operation were made.

Suprapubic prostatectomy was done March 4, 1929. During the first five days the convalescence was satisfactory, temperature and pulse reaching a normal level at that time. Following this the temperature began to rise and on the eighth day after operation the patient had a severe chill followed by a temperature of 105° F. Physical signs revealed evidence of bilateral bronchopneumonia; these were confirmed by roentgen-ray examination. As there was some cyanosis of the lips and finger nails, the patient was placed in an oxygen tent, and oxygen was administered for five days, the concentration being maintained between 47 and 50 per cent. The patient was extremely toxic and drowsy before the oxygen treatment was started, but at the end of twelve hours there was decided improvement in his condition. At the end of five days the temperature and pulse had returned to normal. After a few days the temperature again rose, and there were signs of thrombophlebitis developing in the left femoral vein. There was considerable swelling and pain in the left leg. After ten days, during which the patient had continuous fever and occasional chills, signs of fluid appeared in the left side of the thorax. Five hundred cubic centimeters of bloody sterile fluid were aspirated. Rather marked secondary anemia had developed. The hemoglobin was 40 per cent (Dare), and two transfusions of 500 c.c. of citrated blood were given at seven-day intervals. The patient then recovered gradually and was dismissed on the sixty-fifth day after operation, in excellent condition.

COMMENT

The estimation of the cardiovascular reserve, and improvement of the reserve when possible, bear a distinct relationship to the outcome of operative procedures on the prostate gland. In the study of the cardiovascular system, inquiry should be made into the habits of the patient and the type and amount of physical exertion to which he is accustomed. It is important to know how much fast walking or stair-climbing he can do without the development of dyspnea. The presence or absence of precordial or substernal pain on exertion also should be noted. If a patient is able to do hard physical labor without the appearance of these symptoms, the physician has at once a basis of the estimation of cardiac efficiency. A carefully made general examination, with a consideration of the character of the peripheral arteries, the pulse, the quality of heart tones, and the blood pressure, gives additional information. Electrocardiographic studies have been extremely valuable in adding to knowledge of cardiac disease, and have been of value in estimating cardiac reserve. At times these studies form a relative basis for prognosis and a guide for advising the patient in the future. Case 3 is an example. The patient, although sixty-nine years of age, had been working steadily as a gardener, doing a moderate amount of heavy labor without experiencing any symptoms referable to the heart. The extent of sclerosis of the peripheral arteries was not unusual for his age; the blood pressure was satisfactory, and although the objective examination of the heart reveals some weakness of the tones, serious cardiac disease was not suspected. However, the electrocardiographic data were definite, and indicated serious cardiac disease secondary to arteriosclerosis, and probably coronary disease. The fact that this patient withstood an operation without incident indicates good cardiac reserve. Such a patient should have the benefit of operation and then should be advised as to his activities in the future. If this patient had been suffering from dyspnea, cardiac pain, and hypertension, the danger of operation would have been extremely great.

There is a close relationship between obstruction of the neck of the bladder with resulting renal insufficiency and cardio-

vascular disturbances. However, with drainage of the bladder and the subsequent improvement of renal function, cardiac disturbances often improve quickly. In the more severe forms of cardiac disease, most of which are secondary to arteriosclerosis and hypertension, additional treatment is at times necessary. The institution of complete physical and mental rest, the use of digitalis in selected cases, and the use of diuretics such as ammonium chloride and salyrgan in reducing edema and congestion not only improves the condition of the heart, but aids the general and renal circulation, with resultant improvement of renal insufficiency.

Hypertension in the absence of serious cardiac or renal disease is not a contra-indication to surgical procedures. However, the blood pressure and output of urine should be carefully watched during the first twenty-four hours after operation. A gradual increase in blood pressure with each decade of life may be considered a normal phenomenon. Many patients who have reached the age in which prostatic hypertrophy occurs may have had varying degrees of hypertension for years. As a result, the kidneys have become accustomed to a higher pressure, and the maintenance of this pressure may be essential to proper renal function. Sudden lowering of blood pressure may be followed by decreased output of urine. Such a condition often follows excessive hemorrhage and surgical shock. Maintenance of body fluids is important; it is advisable to give 500 c.c. of a solution of physiologic sodium chloride intravenously just before and just after operation. In the event of a dangerous fall in blood pressure, transfusion of blood should be given and solutions of gum acacia and hypertonic glucose should be administered, with ephedrine, to aid in bringing about vascular equilibrium with resultant improvement of renal function.

Case 4 is an example of other complications which may arise. The use of various types of local anesthesia has been a factor in the reduction of postoperative pulmonary complications. The use of the oxygen chamber and of the oxygen tent seem to have been a factor in the reduction of mortality. Many of the pulmonary complications following operations on the prostate gland

are embolic in origin, and it is in this type of pneumonia that the use of oxygen has been found especially valuable. The mortality rate in such cases has been gradually reduced during the last two decades. This has been brought about by more accurate methods of determining cardiovascular reserve, by careful preoperative preparation, by refinements in surgical technic, and by study and treatment in the individual case.

ROENTGENOLOGIC SIGNS OF POSTOPERATIVE GASTROJEJUNAL AND JEJUNAL ULCER

JOHN D. CAMP

RECURRENT disease and secondary ulceration following gastro-enterostomy constitute a perplexing problem for the roentgenologist. In such cases the examiner should be familiar with the technic of the surgeon who performed the operation, or he should have the assurance that originally the anastomosis was functioning properly. In most instances, however, he has no information with regard to the former and he must assume the condition of the latter, and thus in a certain percentage of cases he subjects himself to an uncontrollable factor of error. Experience in the examination of patients subsequent to gastro-enterostomy has shown that the following roentgenologic signs individually permit a positive diagnosis of gastrojejunal or jejunal ulceration: (1) The presence of an ulcer niche; (2) the presence of a gastrojejunocolic fistula; (3) closure of the stoma, and (4) persistent deformity of the stomach, stoma, or jejunum.

The signs included in the first three groups are obvious and are readily demonstrable by the usually accepted technic for gastro-intestinal examination. They will not, therefore, be considered here. The signs included in the fourth group, although equally diagnostic, are less easily detected, and when elicited, their significance is often perplexing. For this reason certain signs which have been most helpful to me in establishing a diagnosis are presented in the hope that they may facilitate the interpretation of many of the confusing signs that often accompany these lesions.

Deformity of the stomach, usually associated with ulceration at the stoma, is depicted as puckering of the gastric contour and rugae about the site of the anastomosis, with a varying degree

of apparent invagination of the greater curvature at the stoma. This deformity is constant and resists antispasmodic drugs; it is the accepted picture of gastrojejunal ulcer, but the changes do not always prevail. In many cases, the stoma and contiguous portion of the jejunum present a tubular or funnel-like appearance (Figs. 168 and 169) due to obliteration of the usual mucosal

Fig. 168.—Narrowing of jejunum contiguous to stoma, and obliteration of normal mucosal folds, producing so-called tube or funnel sign of gastrojejunal ulcer.

folds by the inflammatory induration that so often accompanies the lesions. The normal continuity of the gastric and jejunal markings (Fig. 170) is interrupted in the involved region. The changes are significant, even though they may affect a small region only. Fortunately they are usually evident on films so that one need not rely on roentgenoscopic evidence alone. In many cases the tube-like change at the stoma is the only significant deformity demonstrable, particularly if there is gastrojejunitis without actual ulceration.

Fig. 169.—Induration at stoma with obliteration of mucosal markings producing "tube sign" of gastrojejunal ulcer.

Fig. 170.—Normal functioning gastro-enterostomy, showing continuity of gastric rugae and markings of jejunal mucosa at the anastomosis.

Deformity of the jejunum has become of increasing importance in the diagnosis of gastrojejunal ulceration, since surgical, pathologic, and roentgenologic observations have shown that the majority of these postoperative ulcers are primarily jejunal in origin. In many instances the roentgenologic changes are confined entirely to the jejunum, and nearly always the efferent loop is affected. Since the ulceration may be found as far as 15 cm. from the stoma, examination should include a good portion of the efferent loop.

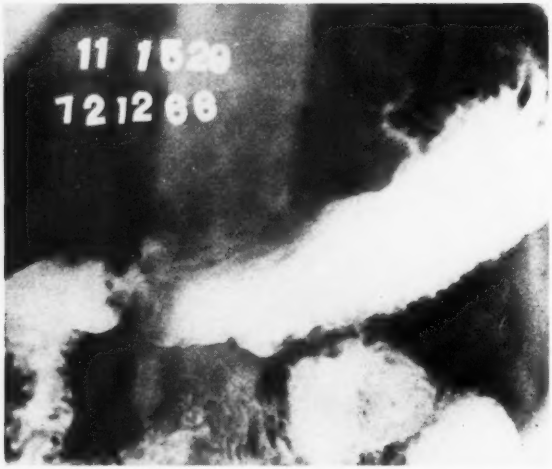

Fig. 171.—Gastrojejunal ulcer, producing persistent narrowing of jejunum just below stoma. There is no deformity of the stomach and stoma.

The deformity of the jejunum may be local or diffuse. The localized change involves only the area near or adjacent to the ulcre, which may or may not reveal itself as a niche. The deformity usually starts at the stoma, and extends 2 cm. or more below it in the efferent loop (Fig. 171). Should the ulceration occur well below the stoma, the portion of the jejunum contiguous to the anastomosis may appear normal. Within the affected region the jejunum is noticeably narrowed or retracted (Fig. 172), and the normal markings of the valvulae conniventes are ob-

literated by the inflammatory reaction. This localized deformity may involve only a small portion and may be easily overlooked. The defect is not unlike the deformity produced by a small annular carcinoma, and it is best shown by roentgenoscopy. Secondary dilatation of the jejunum, proximal, or distal to the defect, is not uncommon. Changes sufficient to cause complete obstruction are rare. When a niche is present it is usually in the

Fig. 172.—Localized narrowing in efferent limb of loop of jejunum produced by a jejunal ulcer.

center of the deformity, and an incisura-like formation is frequently suggested.

Diffuse deformity of the jejunum may involve the afferent as well as the efferent loop (Fig. 173). The affected portion is appreciably narrowed, and the markings of the valvulae conniventes are obliterated. The changes are not unlike spastic segments observed in the colon, especially in regions of incipient chronic ulcerative colitis. Gastric deformity may or may not be associated.

Mechanical conditions that may mislead the examiner consist of adhesions and herniations of the jejunal loop through the opening in the mesocolon. The latter condition is rare, since the practice of stitching the edges of the mesocolon to the stomach has been adopted. Deformities caused by adhesions may be distinguished by the flexibility of the parts, and the presence of

Fig. 173.—Diffuse deformity of afferent and efferent loop of jejunum contiguous to stoma. Gastrojejunal ulcer.

normal gastric rugae and jejunal markings. Outlines of the latter may be distorted, but they will not be obliterated, as is the case in jejunal ulceration. For the distinction of organic defects from those caused by adhesions or atypical surgical technic, nothing can replace careful manipulation under the fluoroscopic screen.

DIFFUSE AMYLOIDOSIS OF UNKNOWN ETIOLOGY

EDWIN G. BANNICK AND NELSON W. BARKER

A PRESUMPTIVE diagnosis of diffuse amyloidosis is not unusual if in a case of long-standing sepsis a clinical picture of the nephrosis type of renal disease develops, especially if it is associated with enlargement of the liver and spleen. In the absence of any associated disease, however, such as sepsis or tuberculosis, which bears etiologic relationship to amyloidosis, and in the absence of hepatic or splenic enlargement, the diagnosis of amyloidosis is rarely considered. Because amyloidosis may occur in this second group of cases and because it can be correctly diagnosed, the following case is reported:

A Mexican, aged thirty-eight years, was admitted to the clinic January 28, 1929. He had been troubled with marked chronic constipation and an indefinite type of dyspepsia with a few symptoms of peptic ulcer for the last four or five years. During this period his general health had not changed and he had continued to work, except for a short period in 1926 when appendectomy had been performed in an attempt to relieve symptoms. After three months of relief from symptoms they again returned and had persisted with very little periodicity. About six weeks before admission, however, he had noticed malaise and gradual failure. Just before Christmas, fever had been noted and this had persisted. Twelve days before admission a mass had appeared in the left side of the neck which had grown slightly and which was somewhat tender. The gastro-intestinal trouble had become much worse and was accompanied with vomiting and anorexia. He had lost 15 pounds in weight in the last month.

The patient appeared ill and toxic. Enlarged, discrete, somewhat tender nodes were palpated in the left anterior cervical

chain extending downward under the clavicle. The spleen could not be felt. The systolic blood pressure was 105, and the diastolic 65. The temperature was of the remittent type ranging from 99° to 103° F.; most of the time it was between 100° and 101° F. The specific gravity of the urine was 1.025; mild albuminuria and an occasional pus cell were noted. Three subsequent urinalyses were entirely negative. The hemoglobin (Dare) was 67 per cent; erythrocytes numbered 4,700,000, and leukocytes varied from 6,700 to 9,500. The differential count was essentially negative. The Wassermann reaction of the blood was negative. Gastric analysis and roentgenograms of the thorax and stomach were negative. One of the cervical lymph nodes was removed for examination and histologic section showed a lymphosarcoma of the Hodgkin type.

Roentgen-ray treatment was given, and because of the vague abdominal symptoms and because the general reaction was somewhat out of proportion to the objective evidence, the entire neck, thorax, abdomen, and back were irradiated. The response to radiotherapy was striking. The vomiting ceased, the temperature dropped, the nodes became smaller, and the patient left the hospital two weeks after admission without fever and with improvement in his general condition.

The patient returned for examination May 29, 1929. Improvement had continued. There had been no recurrence of fever and the nodes in the neck had disappeared. The urinalysis was negative. The systolic blood pressure was 115, and the diastolic 75. The hemoglobin (Dare) was 76 per cent; erythrocytes numbered 4,270,000, and leukocytes 6,800. For five days before admission, however, he had experienced pain and tenderness over the left side of the thorax, and on examination definite tenderness was noted over the eighth and ninth ribs on the left side in the anterior axillary line. Roentgenograms of the ribs, thorax, and thoracic portion of the spine were negative and there was no objective evidence of a local lesion except for the hypersensitiveness. Periostitis was suspected but was not proved. Diathermy had been given without relief; this was followed by another course of roentgen-ray treatment. Because

of the pain in the thorax and slight residual left cervical adenopathy and epigastric tenderness with a questionable small mass deep in the epigastrium, the treatment was extensive. The pain in the region of the ribs disappeared and the patient was dismissed in good general condition.

The patient was readmitted December 12, 1929. He had felt well for several months after dismissal in June and then had begun to fail again. The abdominal distress had returned and in November moderately severe diarrhea had developed, which lasted for several days. Associated with this was nausea and vomiting, which persisted and increased until at the time of admission the patient was vomiting after nearly every meal. He had lost weight and strength rapidly. He was weak and toxic, but not anemic or cachectic. The usual racial pigmentation was present, but excessive pigmentation or unusual distribution were not observed. He was very restless and vomited frequently. The systolic blood pressure was 100 and the diastolic 70; the pulse was of low volume, and the heart tones were faint. There was no significant lymphatic adenopathy. The spleen was not palpated and the edge of the liver was just barely felt on deep inspiration. Masses were not felt in the abdomen and roentgenograms of the thorax, stomach, kidneys, ureters, and bladder seemed normal except for a very small shadow over the upper pole of the right kidney. The stools contained blood, but roentgenograms of the colon were negative. There was no edema or history of edema. Urinalysis disclosed marked albuminuria, mild hematuria, and a few hyaline and waxy casts. The specific gravity of the urine in spite of the severe albuminuria was only 1.015. The excretion of phenolsulphonephthalein was 15 per cent in one hour. The blood urea was 58 mg. for each 100 c.c. The carbon dioxide combining power of the plasma was 54 volumes per cent. The plasma sodium chloride was 544 mg. for each 100 c.c. The hemoglobin (Dare) was 75 per cent; erythrocytes numbered 4,360,000, and leukocytes 8,100. The differential blood count was essentially negative. The serum proteins were 3.8 gm. for each 100 c.c., of which 27 per cent was albumin. The blood cholesterol was 235 mg. for each 100 c.c.

The hematocrit showed 47 per cent erythrocytes and 53 per cent plasma.

The data were unusual for acute glomerulonephritis, and the history was not suggestive of this condition. The absence of edema and anemia, and the presence of low blood pressure would have been most unusual and the patient's condition was too grave to be explained by acute nephritis without a higher degree of renal insufficiency. Also the specific gravity 1.015 of urine loaded with albumin was against acute nephritis.

Subacute or chronic glomerulonephritis could not satisfactorily explain the absence of anemia and the low blood pressure, and again the patient was too sick for the degree of renal insufficiency that could be demonstrated.

Chronic lipoid nephrosis was easily ruled out by the appearance of the patient, the absence of edema, and the presence of hematuria.

Pyelonephritis could be readily dismissed from consideration because of the urinalysis and by the history and appearance of the patient; acute toxic nephrosis could also be dismissed for the same reason.

Because of the unusual renal picture the urine and blood were examined for Bence-Jones protein, but none was found. A Congo-red test was made and it was strikingly positive. More than 75 per cent of the Congo-red that was injected intravenously had disappeared from the blood stream at the end of an hour and the dye appeared only slowly in the urine; at the end of five hours it contained only a small amount. This made the diagnosis of amyloidosis likely and although the liver was not perceptibly enlarged, a test of hepatic function with the bromsulphalein dye showed marked retention of dye, proving extensive involvement of this organ.

In spite of attempts at treatment, the patient failed rapidly and died on the twelfth day after admission. At the end he resembled a patient in the crisis of Addison's disease, with vomiting, extreme restlessness, falling blood pressure, and weak heart sounds. The blood urea on the day before death was 56 mg. for each 100 c.c. A diagnosis was made of diffuse amyloidosis with

renal and hepatic insufficiency and possibility of suprarenal insufficiency.

At necropsy the peritoneal cavity contained 300 c.c. of clear straw-colored fluid. The pleural and pericardial cavities were normal. The heart weighed 230 gm. and was not abnormal. The lungs appeared normal except for slight scarring in the right apex. The spleen weighed 200 gm. It was firm and the cut surface showed symmetric red and grayish-red mottling. The liver weighed 1,490 gm. and was of abnormally firm consistence. A firm white nodule, 1 cm. in diameter, was found in the right lobe. There was superficial ulceration of the lower part of the esophagus. The stomach was normal. There was a healed duodenal ulcer on the posterior wall. The wall of the ileum, cecum, and ascending colon was definitely thickened and firm; there was patchy pseudomembranous enteritis of these regions of the intestinal tract. The pancreas was normal except that there were many hard lymph nodes 1 to 3 cm. in diameter closely adherent to, but not invading, its head. There were several firm white discrete prevertebral lymph nodes 5 to 10 mm. in diameter. The suprarenal glands appeared normal grossly. The kidneys weighed 245 and 250 gm., respectively; they were smooth and pale reddish-brown with moderate obliteration of the markings on the external and cut surfaces. The bladder, prostate gland, testes, thyroid gland, and aorta were grossly normal.

Histologic examination of sections of the heart, lungs, pancreas, prostate gland, and testes was negative. Examination of sections of the pancreatic lymph node, prevertebral lymph nodes, and white nodule in the liver showed numerous large round and polygonal cells scattered in groups through a fibrous stroma with scattered giant cells of the Dorothy Reed type. There were very few eosinophils. Sections of the spleen, liver, kidneys, suprarenal glands, ileum, and cecum were stained with methyl violet and Congo-red for amyloid tissue as well as with hematoxylin and eosin. In the spleen there were large areas of amyloid tissue around the central arteries of the malpighian corpuscles and many scattered small islands of amyloid tissue throughout

between the pulp cells. There was amyloid tissue in the walls of most of the arterioles. There was definite congestion and there were relatively few pulp cells. In the liver there were small deposits of amyloid tissue lining the sinusoids in the peripheral zone of many lobules, and also in many of the arterial walls. The parenchymal cells of the liver were shrunken and atrophic and the sinusoids were dilated in these regions. In the kidneys all the glomerular tufts that were seen contained patches of

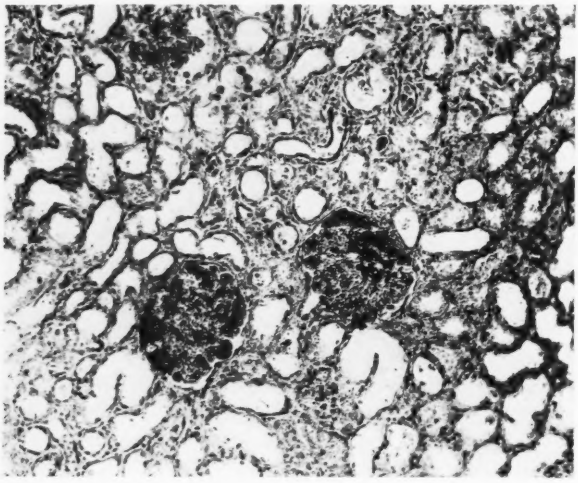

Fig. 174.—Section of kidney. The amyloid tissue shows as black deposits in the glomerular tufts. There is also extensive degeneration and atrophy of the epithelial cells of the convoluted tubules together with some intertubular edema (× 45).

amyloid tissue and in some tufts these were so numerous as to occupy almost all the space inside of Bowman's capsule. There was amyloid tissue in the walls of the small arteries and larger glomerular capillaries. The tubules showed diffuse cellular degeneration and atrophy with many casts and deposits of albuminous material in their lumina. There was slight intertubular edema (Fig. 174). In the suprarenal glands there were extensive deposits of amyloid tissue in the deeper layers of the

cortex with atrophy and disappearance of the cortical cells, but there was a moderate amount of normal cortical tissue near the capsule. In the ileum and colon amyloid tissue was scattered through the mucosa and submucosa. The mucosa was thick and contained many lymphocytes. There were areas of superficial ulceration. The muscularis was thick and hypertrophied. Unstained frozen sections of the spleen, liver, and kidneys showed amyloid tissue faintly but definitely stained with Congo-red, evidence of the intravital staining by the dye given intravenously five days before death.

The anatomic diagnosis was: (1) Lymphosarcoma (Hodgkin's type) of the prevertebral and pancreatic lymph nodes and liver (small nodule); (2) amyloidosis of the spleen, kidneys, liver, suprarenal glands, ileum, and colon; (3) healed duodenal ulcer, and (4) pseudomembranous enterocolitis.

COMMENT

The striking features in this case were: Rapid failure of health for several months with progressive vomiting, but without edema and practically without anemia; profuse albuminuria; mild but definite hematuria; marked reduction in excretion of phenolsulphonephthalein; slight retention of the urea in the blood; low blood pressure; small heart; absence of retinitis; decrease in the serum proteins; inversion of the albumin and globulin ratio, and a slight increase in the blood cholesterol.

The case presented data that were atypical for any ordinary form of nephritis or nephrosis and it was deemed advisable to exclude the other possibilities. Attention has previously been called to this form of reasoning in making a correct diagnosis in unusual cases of Bence-Jones proteinuria and renal insufficiency.[1] In this case both the urine and blood were negative for Bence-Jones protein.

The next possibility to be considered was that of renal amyloidosis. This could explain the data satisfactorily, but there seemed to be no reason for the occurrence of amyloidosis. The Congo-red test gave somewhat surprising results and a diagnosis of amyloidosis was made.

The Congo-red test was first described by Bennhold in 1923, who found that a solution of Congo-red injected intravenously was normally excreted by the liver over a period of approximately twenty-four hours. The normal rate of disappearance from the blood stream measured by colorimetric comparisons of the blood serum was found to average 19 per cent of the amount injected in the first hour, assuming that three to six minutes after injection 100 per cent of the dye is uniformly distributed throughout the blood stream. In certain types of renal disease some dye is excreted in the urine in the first hour after injection, but this never exceeds 3 per cent of the amount injected; hence it does not materially affect the percentage rate of disappearance from the blood stream. Bennhold reported the results of tests in 100 cases and found that in only one condition, amyloidosis, was there definite acceleration of the rate of disappearance of the dye from the blood stream. In these cases 60 to 100 per cent of the dye disappeared in one hour. He explained this by the strong absorptive affinity of amyloid tissue for Congo-red and demonstrated vital staining of this tissue by the dye at necropsy seven weeks after the test had been made. He concluded that the test was specific for amyloidosis provided there were extensive deposits of amyloid tissue in the body particularly in the liver. His results have been confirmed by other observers and the test is the only one described for a definite clinical diagnosis of this disease. In making these tests at the clinic, we have used 18 c.c. of a 1.5 per cent solution of the dye freshly prepared in triple-distilled water and boiled for one minute. The normal rate of disappearance, judged from the results in twenty-nine cases, varied between 10 and 39 per cent with an average of 22 per cent in one hour. It is believed that a rate of disappearance of more than 60 per cent is indicative of extensive amyloidosis and therefore the diagnosis in this case was made when it was found that more than 75 per cent of the dye had disappeared from the blood stream in one hour.

The etiology of the amyloidosis in this case remains unknown. The rather extensive roentgen-ray treatment was considered as a possible causative factor. It was not possible to find in the

literature anything to confirm this idea. Neither was a record found of a similar case due to lymphosarcoma. In this case the lymphosarcoma was not extensive and the febrile course was short.

CONCLUSIONS

1. Diffuse amyloidosis of unknown etiology may occur.

2. The diagnosis in such cases can be correctly made even though the liver and spleen are not enlarged. The diagnosis is usually suggested by the condition of the kidney.

3. The clinical picture of renal amyloidosis is that of chronic nephrosis which may simulate lipoid nephrosis, but which usually differs somewhat in that there is likely to be some hematuria and more reduction in the excretion of phenolsulphonephthalein; edema, hypercholesterolemia and decreased serum proteins are variable factors. There is a pathologic basis for these differences in that the most extensive amyloid deposits in the kidney are in the glomeruli.

4. A Congo-red test which shows disappearance of more than 60 per cent of the dye from the blood stream in one hour is practically specific for diffuse amyloidosis.

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INTERMITTENT CLAUDICATION IN THE EXTREMITIES WITH PULSATING VESSELS

BAYARD T. HORTON

INTERMITTENT claudication is the most significant symptom in the diagnosis of occlusive vascular disease affecting the extremities. It was first described in man by Charcot in 1858. He had previously called attention to an affection in horses that had its analogy in man, and to which he had given the name "intermittent claudication." Baullay apparently first described this condition in the horse in 1831; Erb gave a classic description of the phenomenon in 1892. It is not a disease as described by earlier writers, but merely a symptom. It may manifest itself as a cramp-like pain or as a feeling of distress following exercise and may be localized either in the upper or lower extremities. Frequently, only a certain group of muscles seems to be involved. In the lower extremities, the distress is usually confined to a single digit, to the arch of the foot, or to the calf of the leg. In the upper extremities, either a digit, the entire hand, or the forearm may be the site of the distress. The characteristic feature of the pain or distress is the fact that it invariably comes on after exercise and is relieved by rest. Many patients can state the number of steps or the amount of exercise necessary for production of pain, and the necessary period of rest required for relief. More than 50 per cent of patients with thrombo-angiitis obliterans admitted to The Mayo Clinic give a history of intermittent claudication, but in the great majority there is closure of one or more of the usual palpable arteries in the extremities. It is extremely rare to find all of the palpable arteries pulsating normally. The same statement is true with reference to occlusive vascular disease of the extremities on an arteriosclerotic basis, although this syndrome is more commonly found in the latter group of cases than in cases of thrombo-angiitis obliterans.

I have never seen intermittent claudication in a case of Raynaud's disease or in cases of vasomotor neurosis of the vasoconstricting type. It is doubtful if it ever occurs. If intermittent claudication is present, I feel that it is indicative of an underlying occlusive vascular process, which, however, may not be detected by palpation of the usual palpable arteries in the extremities. The occlusive process may be in the finer arterioles, with the main arterial trunks pulsating normally. Zak and others have shown that intermittent claudication can be produced after exercise in a normal upper or lower extremity, when the main artery to the extremity (brachial or femoral) is artificially compressed. An explanation of the phenomenon, other than that reflexes originate in diseased vessels themselves, must be looked for. The most recent opinions tend to the acceptance of an explanation based on chemistry, and the distress or pain is explained on a basis of anoxemia. Lactic acid and other fatigue-substances are formed when a muscle contracts. Shaffer says that the sudden explosive formation of lactic acid is the essential agent causing muscular contraction. Under normal conditions the lactic acid is largely reconverted into glycogen, whereas with an inadequate blood supply it tends to accumulate in the muscles, although it is partially neutralized by alkaline salts and buffer substances. The rapidity of its disappearance from the active muscle apparently depends on the arterial blood flow. If the arterial blood supply is inadequate, as it is in occlusive vascular disease, the lactic acid tends to accumulate in the muscle, and symptoms of fatigue or pain develop.

The importance of intermittent claudication as a diagnostic symptom and the difficulties sometimes encountered in the diagnosis of vascular diseases affecting the extremities are illustrated by the following cases.

Case 1.—A man, aged sixty-four years, of American extraction, registered at the clinic, January 18, 1929, complaining of distress in the feet, associated with exercise and relieved by rest. This train of symptoms had been present for about twelve years, and had remained more or less stationary during this time. He

had undergone tonsillectomy in 1918, and had been a moderate smoker for many years.

Twelve years before admission he had noticed that pain appeared in the insteps of both feet each morning as he walked from his home to the railroad station, a distance of ten city blocks. This pain had appeared at the end of five blocks, and he described it as feeling as if "the tendons or fascia of the feet were being pulled apart." However, the pain had not been sufficient to cause him to stop walking and he had continued the distance of ten blocks, although he had been uncomfortable all the rest of the way. During the day's work he had not experienced discomfort in the feet for he had remained in his office most of the time, but the pain had returned each afternoon as he walked from the station back to his home. These symptoms gradually had increased in severity, despite all sorts of treatment, including the use of arch supports with special orthopedic shoes, osteopathic and chiropractic treatments, hot-water baths, dieting, massage, ultraviolet light, electricity, diathermy, medicines of various types, and Christian Science. About four years before admission he first had noticed an aching feeling in the calves of the legs, associated with the pain in the feet following excessive walking. It had seemed to appear in both legs at the same time. At the time of admission he could walk about two blocks without discomfort. Then the pain in the instep began, and increased, so that by the time he had gone the third block, the pain was very severe. Complete relief was obtained by sitting down, or by stopping and alternately raising first one foot and then the other from the ground for a short time. In order to get complete relief, it was necessary to remove the weight of the body from the feet. Frequently he had difficulty in playing the first five holes of golf because of the pain in the arches of the feet. This would be relieved by rest, and after that he could play eight or ten holes of golf without very much discomfort. Prior to admission he had consulted twenty-five physicians, and had spent approximately ten thousand dollars for medical advice. The diagnosis in most instances had been "arthritis."

The general examination disclosed nothing of great impor-

tance. The patient's height was 5 feet and 8 inches and his weight 174 pounds. He appeared to be in perfect health. The blood pressure was 126 systolic and 76 diastolic, and the heart was of normal size. The neurologic examination revealed fibrillary twitching of the soles of both feet, and some atrophy of the muscles of the calf of the left leg. The neurologic diagnosis was abiotrophy, which it was thought had no direct relationship to the complaints of pain in the feet. The orthopedic surgeons stated that the feet were structurally perfect. The vessels of the hands pulsated normally, as did all of the palpable vessels in the lower extremities, with the exception of the dorsalis pedis and posterior tibial arteries. They were approximately 50 per cent closed, although the pulsations were still good. There was no demonstrable rubor with the feet in the dependent position, and no blanching with the feet elevated. Trophic changes were not present.

Roentgenograms of the legs and feet disclosed evidence of calcification of the larger vessels whereas those of the thorax revealed hypertrophic arthritis of the thoracic part of the spinal column. Roentgenologic examination gave evidence of two infected teeth. Urinalysis and the Wassermann reaction of the blood gave negative results. The concentration of hemoglobin was estimated at 81 per cent by the Dare method; erythrocytes numbered 4,680,000, and leukocytes 9,000 in each cubic millimeter of blood. The concentration of uric acid in the blood was 5.5 mg. for each 100 c.c. and the viscosity of the blood was 6.4 (normal 4.5). Return of phenolsulphonephthalein in the urine was 65 per cent in two hours. Examination of the ocular fundi gave negative results. The vasomotor index in the left foot was 5.2 and that in the right 9.6.

This case presents unusual features: First, the history of having had, for twelve years, pain on exercise in the arches of both feet in the presence of open vessels and in the absence of trophic changes; second, the slowly progressive nature of the disturbance, and its bilateral symmetric distribution, and third, the partial, and at times, complete, disappearance of the pain in the arches after continued walking. The disappearance of the

pain may be accounted for on the following basis: A certain amount of spasm may be present under conditions of rest, and it may be released by exercise; the high vasomotor indices would seem to reënforce this possibility. The prognosis in this type of case must be very good. It was suggested that the patient carry out postural exercises and contrast baths daily and continue his walking exercise to the point of tolerance. He was also given instructions regarding the prophylactic care of his feet.

Case 2.—A man, aged seventy-one years, of French and Irish descent, registered at the clinic, January 9, 1929, complaining of pain in the feet and legs, associated with walking, and followed by prompt relief with rest. These symptoms had begun three years before he came to the clinic and had gradually increased in severity. At the time of admission, he could walk only the distance of two city blocks without cramps in the calves of the legs. The pain was sufficient to cause him to stop walking; he would rest for a minute or two, would get complete relief in this way, and then would continue walking for a similar distance. In the last year also he had experienced a burning sensation in the feet, if he walked, or even if he stood for any length of time. The family history was negative, except that his father, three uncles, and two aunts had had diabetes mellitus. He had had no operations and his general health had always been good. He had smoked from eight to fifteen pipefuls of tobacco daily for many years.

General examination revealed a rather obese man, 5 feet and 11 inches tall, and weighing 196 pounds. There was generalized arteriosclerosis of all the palpable vessels, and examination of the ocular fundi also disclosed sclerosis, graded 2, of the retinal vessels. There was dental sepsis, graded 2. The remainder of the general examination was essentially negative. All of the palpable vessels in the hands and lower extremities pulsated normally. There was no blanching with the feet elevated, but there was rubor, graded 2, with the feet in the dependent position. The feet felt cold to the touch, although the patient complained of a slight burning sensation in them at the time of the

examination. He had been walking just before the examination. This burning sensation was not present while he was in bed or was at rest for any length of time. Neurologic examination gave negative results except for a diagnosis of arteriosclerosis of the central nervous system. The blood pressure was 152 systolic and 76 diastolic. Examination of urine, the Wassermann reaction of the blood, and roentgenograms of the thorax all gave negative results. The concentration of blood sugar was 11 mg. in each 100 c.c. The concentration of hemoglobin was 64 per cent by the Dare method; erythrocytes numbered 3,980,000, and leukocytes 5,700 in each cubic millimeter of blood. Roentgenograms of the feet and legs gave evidence of calcification of the larger vessels.

A diagnosis of occlusive vascular disease of the lower extremities on a basis of arteriosclerosis seems justified in this case. The history of intermittent claudication cannot adequately be explained on any other basis. The occlusive process in this case must be similar to that in Case 1. A reduction diet and a protective regimen for the feet was outlined for the patient. The prognosis was fairly good.

Case 3.—A small, frail woman, aged seventy-four years, registered at the clinic, August 20, 1928, complaining of "foot trouble" when she walked. Her father had died with pulmonary tuberculosis at the age of sixty-seven years. A diagnosis of pulmonary tuberculosis had been made in her case when she was thirty-four years of age. She had gone to New Mexico for treatment and since had made her home there. She had been married thirty-eight years, but had had no children or pregnancies. In 1922 she had undergone cholecystectomy with uneventful recovery. Five or six years before she came to the clinic she first had noticed pain in the feet after walking or standing. She had been free from pain when she was not on her feet. These symptoms had recurred at intervals, but gradually had seemed to become worse. Thirteen months before she presented herself for examination she had had an attack of "rheumatism," with pains over the entire body, but mostly in the back and hips.

This had been especially noticeable when she moved in bed. There had been no pains in the feet. For the eight months prior to her coming to the clinic she had had pain in the muscles of the calves of both legs when she walked. This was relieved by rest. The pain was worse in the left leg, and came on at the end of fifty to one hundred yards of walking. After resting for a minute or so, she could continue for a similar distance, when the pain would recur. Three months before she had come to the clinic she had fractured the bones of the right arm; she had been in bed for one month, and, after she had gotten up, the pain in the feet and legs had seemed much worse. She could walk only about twelve steps without pain. At the time of admission she could take only fifty steps without pain in the muscles of the calf of the left leg.

General examination disclosed evidence of marked loss of weight. The patient was 5 feet and 1 inch tall and weighed 98 pounds. Examination of the fundi revealed sclerosis, graded 2. The tonsils were infected and all of the teeth had been extracted. There was bronchial breathing at the apex of the right lung, and a few râles were present. Examination of the heart gave negative results and the remainder of the general examination was essentially negative, except for the condition in the extremities. There was a flexor contracture of the left hand and fingers, following the old fracture, and disuse atrophy, graded 2. Also motion of the left elbow was limited, due to an old injury. The vessels of the hand on the right side pulsated normally, but the left radial artery was partially closed and no pulsations could be felt in the left ulnar artery. All the arteries in the lower extremities pulsated normally, except the pedal and posterior tibial arteries. They seemed diminished 25 to 50 per cent. With the feet elevated there was blanching, graded 1, and with the feet dependent rubor, grade 1, of the toes.

Hourly readings of blood pressure taken over a period of twenty-four hours indicated a systolic range of 130 to 170 and a diastolic range of 80 to 90. Examination of the urine and the Wassermann reaction of the blood gave negative results. The concentration of the blood urea was 40 mg., of creatinine 1.8

mg., and of blood uric acid, 4 mg. in each 100 c.c. The concentration of hemoglobin was estimated at 65 per cent by the Dare method; erythrocytes numbered 3,820,000 and leukocytes 10,000 in each cubic millimeter of blood. Roentgenograms of the thorax disclosed evidence of an old, calcified tuberculous process at the apex of the right lung, and roentgenograms of the kidneys, ureters, and bladder gave negative results. A roentgenogram of the right arm gave evidence of osteoporosis of the humerus, ulna, and radius. The roentgenogram of the legs was negative for calcified vessels and osteoporosis.

During the patient's stay of ten days in the hospital she was treated with postural exercises, contrast baths, and radiant heat, and at the time of her dismissal she could walk from 200 to 300 yards without discomfort in the legs. It is doubtful if she will improve much beyond this point.

Case 4.—A Russian Jew, aged fifty-two years, registered at the clinic, January 18, 1929, complaining of pain in the calves of both legs after walking. This had been present for fifteen months. He had been an excessive cigarette smoker since childhood, and at the time of admission he was smoking fifteen cigarettes daily. For a period of fifteen months he had observed gradually increasing symptoms of fatigue in the calves of both legs after walking. The symptoms were more marked in the right leg and had appeared sooner there than in the left leg. At first, he described the sensation as a "tired feeling" in the calf of the leg, but this symptom had gradually been replaced by a sensation of pain at the end of five to six blocks of brisk walking. Rest had brought prompt relief, and the patient then had been able to resume walking. After he had walked a similar distance, however, pain had recurred and had seemed to be sharper. There was no history of superficial phlebitis.

General examination revealed a well-developed and well-nourished man, 5 feet and 5 inches tall, weighing 158 pounds. The examination was essentially negative except for the extremities. Foci of infection were not present. The teeth and tonsils had been removed elsewhere. The radial and ulnar

arteries pulsated normally, and pulsation in both lower extremities (femoral, popliteal, dorsalis pedis and posterior tibial arteries) was normal in all vessels with the exception of the vessels in the feet, where pulsation of the dorsalis pedis and posterior tibial arteries was reduced approximately 50 per cent. With the feet elevated, there was blanching, graded 2, and with the feet in the dependent position there was rubor, graded 1. The feet were warm when examined at ordinary room temperature. Trophic changes were not present. The laboratory tests were negative; they included urinalysis, blood counts, Wassermann reaction of the blood, and roentgenograms of the legs for calcified vessels.

The patient was placed on the usual regimen for this vascular condition, which consists of postural exercises, contrast baths, the use of radiant heat, and intravenous injections of triple typhoid vaccine. This regimen is being carried out at the patient's home, and the prognosis in this case seems good.

A tentative diagnosis of thrombo-angiitis obliterans seemed warranted in view of the patient's age, nationality, absence of demonstrable sclerosis of the vessels by roentgen ray, the positive circulatory test, and the history of intermittent claudication. It is definite that he has an occlusive vascular disease and it is more probably due to thrombo-angiitis obliterans than to arteriosclerosis.

Case 5.—A man, aged fifty-seven years, of American extraction, registered at the clinic, April 8, 1929, with the chief complaint of pain in both thighs after walking a short distance. The pain was followed by prompt relief if he rested. This had been first observed eighteen months prior to admission, but had persisted only for a day or so. After this, he had been free from symptoms for nine months, when the distress had recurred. At first he had been able to walk a distance of five city blocks, at which time he had begun to have an exhausted feeling in the posterior femoral muscles. If he continued to walk, he had had pain. The exhausted feeling had seemed to begin about the rectum, spreading to the thighs and sacrum. These sensations

had been symmetric in distribution and had been promptly relieved by rest. He stated that he never had had any discomfort or pain while sitting or lying in bed. At the time of admission he could walk the distance of only two to three city blocks without distress. Rest gave complete relief; thereafter he could walk a similar distance, but the distress recurred. At times he described the distress as a dull, aching pain. There was no history of superficial phlebitis. He had been a moderate smoker since the age of nine years.

The patient was approximately 5 feet and 7 inches tall and weighed 180 pounds. The blood pressure, taken at hourly intervals over a period of twenty-four hours, with the patient moderately active during the waking hours, disclosed a systolic range of 152 to 190, and a diastolic range of 85 to 130. The general examination was essentially negative except for retinal and peripheral arterial sclerosis, graded 1, compensatory cardiac hypertrophy, the presence of a small polypoid fibrous tumor on the left vocal cord, which was found incidentally, and the condition of the extremities. The pulsations in both radial arteries were normal, but pulsation in the ulnar arteries was diminished 50 per cent. All of the palpable arteries in the lower extremities pulsated, but pulsations were reduced 25 per cent. Results of the circulatory test in the feet were negative. Examinations of urine gave negative results except for an occasional trace of albumin. The blood counts were normal and the Wassermann reaction of the blood was negative. There were no significant changes in the electrocardiogram. Roentgenograms of the sinuses, thorax, kidneys, ureters, and bladder all gave negative results. A roentgenogram gave evidence of slight arthritis of the lumbar part of the spinal column with sacralization of the fifth lumbar vertebra on the left side and marked calcification of the pelvic vessels. Roentgenograms of the legs were entirely negative for calcified vessels. Neurologic examination was negative except for mild arteriosclerosis of the central nervous system. The neurologist regarded the patient's pain as true intermittent claudication.

The tumor of the vocal cord was removed under local anes-

thesia, and the patient made an uneventful recovery. During his stay of two weeks in the hospital, he received four intravenous injections of triple typhoid vaccine in addition to contrast baths, postural exercises, and radiant heat. At the time of dismissal he was able to walk a distance of six city blocks without discomfort.

Case 6.—A man, aged fifty-nine years, of English and American extraction, came to the clinic, January 15, 1929, complaining of pain in both legs after walking. Four months prior to admission he had had sharp pain in the muscles of the right hip, and on the following day a similar attack of pain in the left hip. He had been in bed four days and had not left his home for a period of ten days. When he had attempted to walk, he had experienced a dull, aching pain in the posterior femoral group of muscles. This pain had become worse as he had continued to walk, and he had had to stop and rest at the end of 400 yards. He had obtained prompt relief when he had sat down for a minute or so. A longer period had been required to obtain relief if he had remained standing. This syndrome had recurred after the period of rest if he had walked another 400 yards. These symptoms had gradually increased in severity, and a few weeks prior to admission he had had cramp-like pains in the muscles of the calves of both legs, in addition to the pain in the posterior femoral muscles. The pain had developed first in the thighs and later in the legs. Rest always had produced prompt relief. At times, he had experienced this same cramp-like pain if he had remained standing for any length of time while carrying on a conversation. Sitting for a minute or so had given prompt relief. He had been unable to work for six weeks prior to admission.

The patient was 6 feet in height and weighed 154 pounds. He appeared to be in good health. Nothing significant was disclosed by the general examination except sclerosis, graded 1 to 2, of the peripheral arteries. All of the palpable arteries in the upper and lower extremities pulsated normally except the dorsalis pedis on each side; pulsations in them were diminished approximately 50 per cent. The circulatory test was negative ex-

cept for rubor of the toes, graded 1, with the feet in the dependent position. The feet felt warm. The blood pressure was 120 systolic and 90 diastolic. Examination of urine gave negative results; blood counts, and chemical examination of the blood gave results within the range of normal and the Wassermann reaction of the blood was negative. Viscosity of the blood was 4.7. Roentgenograms of the skull, thorax, lumbar part of the spinal column, and pelvis all gave negative results. Roentgenograms of the legs disclosed definite calcification of the larger arteries.

The patient remained in the hospital for a period of nine days during which time he received four intravenous injections of triple typhoid vaccine, with good reactions each time. In addition to the vaccine, he received contrast baths and carried out postural exercises. The pain on exercise improved at least 50 per cent following this treatment. Follow-up letters indicate that he is still improving.

COMMENT

It is interesting to compare Case 5 with Case 6. In both there was intermittent claudication in the posterior femoral group of muscles, and in addition, in Case 6 there was intermittent claudication in the muscles of the calves. The roentgen rays disclosed calcification of the pelvic arteries in Case 5, and none in the legs, whereas roentgenologic examination gave no evidence of calcified vessels in the regions of the pelvis and thighs in Case 6, but disclosed calcification of the vessels of the legs. Positive roentgenograms are helpful in the making of a diagnosis of occlusive vascular disease, but negative roentgenograms do not rule out this condition. The positive vessels, however, frequently pulsate normally. It seems logical to assume that the occlusive process in the six cases which have been presented in this paper was confined to the smaller arterioles and probably accounts for the vascular insufficiency which is present during exercise.

The diagnosis of occlusive vascular disease of the lower extremities seems justified in these cases, and I do not believe the pain on exercise in the arches of the feet, and in the legs and

thighs, can be adequately explained on any other basis. It should be emphasized that a positive circulatory test indicates occlusive vascular disease in an extremity, but a negative test does not, and cannot, rule out this condition. The usual belief

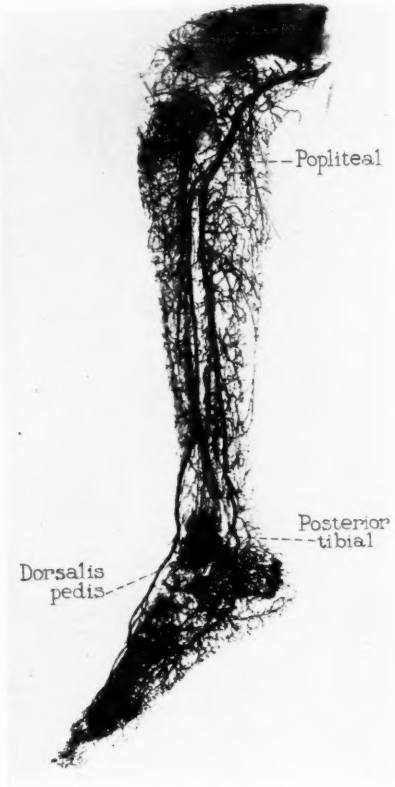

Fig. 175.—The appearance of the normal arterial tree in the leg and foot.

is that good pulsations in the palpable vessels of an extremity (Fig. 175) and a normal, or at least adequate, blood supply, are synonymous terms, and that the latter necessarily follows if the pulsations are at all within normal range. Clinical experience

seems to have justified this belief. And yet, I can conceive of the palpable vessels being open and the smaller vessels so occluded that one would experience pain on exercise, even after moderate exercise. This is well illustrated in Figure 176, in

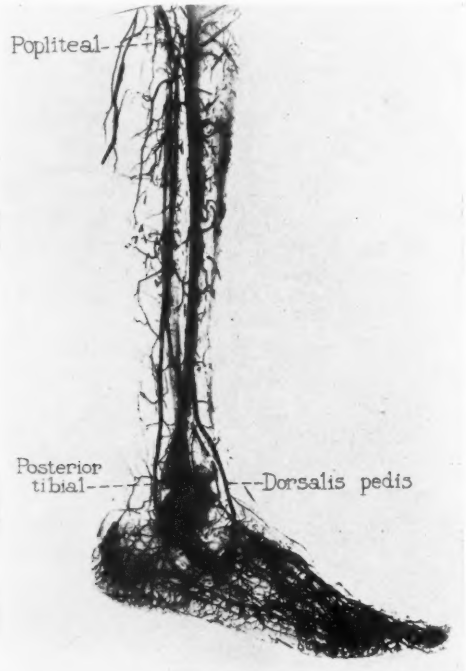

Fig. 176.—The arterial tree in this case was originally photographed to illustrate the absence of collateral circulation in a case of arteriosclerosis. It serves, also, to illustrate the basis for the development of intermittent claudication in the calf muscles. In such a case the main arteries would continue to pulsate. The patient was a man aged sixty-two years.

which the main vessels to the leg are open, but the finer branches are occluded. This same vascular tree can adequately explain the clinical picture which these cases present. Figure 177 represents just the opposite type of picture, in which the main vessels below the popliteal artery are entirely occluded, whereas

the collateral circulation is sufficient to nourish the tissues. One finds all degrees of variation between these two extremes.

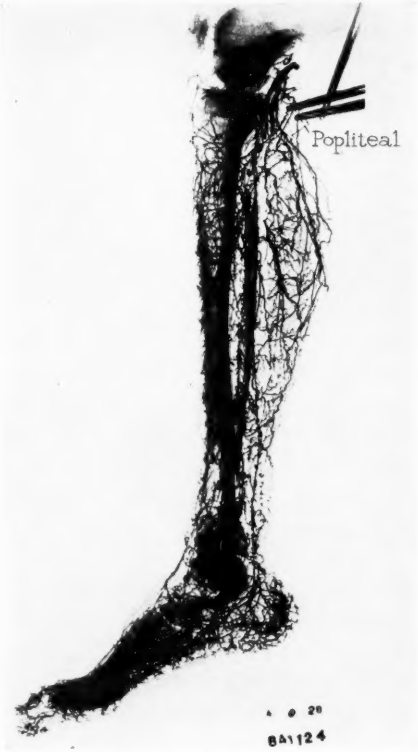

Fig. 177.—Arterial tree in a case of arteriosclerosis. The main vessels are occluded below the popliteal; collateral circulation is well developed. The patient was a man aged sixty-nine years.

MILD DIABETES AND SEVERE DIABETES

MARTIN PATMOS, ELMER C. BARTELS, AND S. FRANKLIN ADAMS

WE are not in sympathy with the idea that diabetes is a mild disease. This implies that severe diabetes is the exception rather than the rule, and although this may be partly true, it may lead physicians and patients alike to underestimate the seriousness of the disease. Most patients with diabetes are aged more than forty years and in general the older patients have a mild form of the disease. But it must be remembered that insulin is enabling many patients to live who otherwise would die, and before long there will be many patients with diabetes, who, at the age of forty years, will have had diabetes for fifteen years. If this disease has existed for fifteen years it is assumed that it is mild and innocuous in character, but it is not necessarily mild.

We wish to present both sides of the situation: (1) Older patients who have had diabetes for twenty years or more, of the milder type, and (2) younger patients who have had a severe form of the disease. It is the second group which will become more important as time advances, and by studying the first group one may discover what is in store for the second. The reader is not to infer that the cases reported here had been under continuous observation during the whole course of the disease, but all of these patients appeared at the clinic some time during the last fifteen years; their progress has been noted by correspondence and by personal visit.

MILD CASES

In twenty-seven cases the diabetes was mild. If one calculates the expectancy of life from the age at which diabetes began in the six fatal cases in this group, one finds that the patients actually lived to be an average age of sixty-four and eight-tenths

years as against the average expected age at death of sixty-seven and one-tenth years, and they had had diabetes for an average period of twenty-five and seven-tenths years. Two patients of the six who died actually outlived their life expectancy calculated from the age when the diabetes began.

The twenty-one survivors became diabetic at the average age of thirty-five years. They are now an average of sixty-one and eight-tenths years. As a group, they have three and two-tenths years to live to fulfill their life expectancy as of age thirty-five. Six of these patients have already lived or outlived their life expectancy.

Only nine of the twenty-seven patients in this group are women. The preponderance of men may be due to the fact that prior to 1909 many more men than women were being examined for life insurance, and the chance of accidental discovery of sugar in the urine was therefore greater, or because prior to 1909 women were less likely than men to discuss such symptoms as polyuria, or because as bread winners men were more likely to demand and to receive greater consideration as regards their health.

Since the average age of patients in this series is now sixty-one and eight-tenths years, it is not surprising to find arteriosclerosis in the arteries of the extremities, the heart or the retinal vessels. Sclerosis was easily demonstrable in eighteen cases. During the early years of their disease the type of food which they ate is not accurately known, but for the last few years many of them have been instructed to eat food relatively high in fat, but with the total calories limited, as a rule, to 2,300. We are not convinced that these patients show more arteriosclerosis than persons of comparable age without diabetes.

It will be remembered that these patients had diabetes at least thirteen years before insulin was available. Since 1922, when insulin was introduced, twelve of these patients have taken insulin, but insulin has been used as a rule in considerable amounts only during the course of an infection. There are only a few patients taking insulin regularly, and the daily dose used by these rarely exceeds 20 units.

Coma occurred in three cases of this series. Two patients

died in coma. Coma can occur even in the mild cases of diabetes, and it is a constant threat. So far as we know, twenty-four patients evidently had diabetes for at least twenty years without ever having had coma. At some time during this period, some of them must have been indiscreet from a dietetic point of view, and yet they were fortunate enough to escape the hazards of ketosis.

Seven patients had gangrene of the feet. One would expect the incidence of gangrene to be high in this group, yet twenty patients have had diabetes for twenty years or more without the development of gangrene.

Twelve of the patients showed some sclerosis of the retinal vessels, but only five had changes characteristic of retinitis of diabetes. Five patients had not had special examination of the eyes. Four patients had opacity of the lens. Eight patients had had diabetes for at least twenty years and are entirely free from any pathologic changes in the eyes.

Six patients died; the cause of death may be classified as preventable or unpreventable. In two cases death was probably preventable. In one case, insulin was stopped because it was believed to be producing blindness when, as a matter of fact, there was probably a shift in the blood sugar level with resulting myopia. In the other case, the diet was followed irregularly.

SEVERE CASES

Seventy-two patients had had diabetes for an average of five and eight-tenths years. The average age in the group is now twenty-nine and four-tenths years. With a few expections the patients are eating food limited to about 70 gm. of carbohydrate and a "G" or glucose equivalent of 120 gm. On such a diet they are able to keep the urine comparatively free from sugar only by taking at least 50 units of insulin a day. If one unit of insulin burns 2 gm. of glucose, a minimal estimate under normal conditions, it appears that these patients eating 120 gm. of total glucose have a so-called "natural" tolerance for only 20 gm. of glucose under these conditions. Life expectancy in this group was forty years at the average age when the patients became

diabetic. The patients have lived five and eight-tenths years. Thirty-three are females and thirty-nine are males.

Clinically demonstrable arteriosclerosis appeared in seven of the cases of severe diabetes. The average age of the patients with arteriosclerosis is fifty-nine years. We have searched carefully for evidence of sclerosed vessels, in the young patients, and except for an occasional patient with "narrowing of the choroidal vessels" we have not observed premature sclerosis of the walls of the vessels. We shall continue to watch for the development of changes in walls of vessels in our younger patients. It is too soon to draw conclusions from the continuous effect of a diet relatively high in fat. Up to the present time, however, after more than five years' experience with the diet such as Wilder proposed, we see no reason to change because of the premature development of arteriosclerosis.

Coma occurred in seven of the cases. One patient was admitted to the clinic in coma; the other six either were in coma shortly before admission or after they had been under treatment for a time and infection had developed. One patient, a man aged fifty-eight years, died in coma.

Two patients had gangrene, a woman aged fifty-one years and a man aged sixty-three years. One would not expect much gangrene in patients whose average age is twenty-nine and four-tenths years.

Thirteen patients exhibited some abnormality of the eyes. The younger patients had lipemia retinalis and the older patients

TABULATION

COMPARISON OF VARIOUS ASPECTS OF THE TWO TYPES OF DISEASE

	Cases.	Sex.		Present average age, years.	Duration of diabetes, years.	Incidence of coma.		Gangrene, cases.	Changes in the eye, cases.	Incidence of arteriosclerosis, cases.	Deaths.
		Male.	Female.			Cases.	Per cent.				
Mild cases....	27	18	9	61.8	25.7	3	11.1	7	19	18	6
Severe cases..	72	39	33	29.4	5.8	7	9.7	2	13	7	9

had changes in the lens or choroidal vessels. Fifty-nine patients were free from any ocular changes.

The tabulation on page 802 shows the comparison of various aspects of the mild and the severe cases.

SUMMARY

Diabetes is a disease of varying severity. We have herewith presented two groups of cases, those of a mild type and those of a severe type of the disease. We wish to emphasize the point that diabetes of any degree is to be regarded as an ever-present threat. In three of twenty-seven cases of mild diabetes coma developed and in seven of seventy-two cases of severe diabetes coma developed. It is significant that the incidence of coma in the cases of mild diabetes and in the cases of severe diabetes is about the same.

It appears that the incidence of severe diabetes is about equal among men and women. In the cases of mild diabetes there were twice as many men as women.

Arteriosclerosis is common in older patients with a mild type of the disease, as would be expected. We shall continue to watch the younger patients for the development of thickening in walls of the vessels. Thus far the amount of arteriosclerosis in the younger patients with severe diabetes is not impressive.

The majority of the older patients had changes in their eyes; only a few of the younger patients had such changes.

PURPURA OF INFECTIOUS ORIGIN (URTICARIA HEMORRHAGICA)

LOUIS G. STUHLER AND ALLEN C. NICKEL

PURPURA has been associated with trauma or varicosities; with dietary deficiencies such as those which result in scurvy; with dietary idiosyncracies, such as some persons have to wheat bread, milk, sugar, or egg; with the giving of salvarsan, benzol, or phosphorus; with snake bites; with diseases of the central nervous system, such as tabes or multiple sclerosis; with numerous infections, and with other heterologous conditions. As one author stated, these different types can be classified very easily, but when discussion arises concerning them they appear not to be discrete but tend to merge. Naegeli stated that one should always associate purpura with some possible systemic involvement. Of especial interest are those forms of purpura that are related to the hematopoietic system.

Purpura hemorrhagica is recognized as a clinical entity, has definite clinical characteristics, and in certain stages can be treated successfully. However, regarding its primary etiology very little is known. According to Whipple, "the etiology of purpura hemorrhagica is not known, the pathology is ill-defined and the differential diagnosis is at times difficult." Various writers consider it a manifestation of a deranged reticulo-endothelial system, but not a disease entity. That remissions may occur, associated with infections, is significant. Whipple stated: "It may be that the poisons from bacteria may stimulate some element in the reticulo-endothelial system to an excessive thrombocytolysis. This factor of infection is a most important one and may be the underlying cause even in the so-called 'idiopathic' purpura cases." We wish to report the following case, since infection seems to be its dominant factor.

REPORT OF CASE

A married man, aged forty-six years, entered The Mayo Clinic in September, 1929. He had been in good health until six years before, when suddenly, in the afternoon, the left hand had begun to swell, and by night he had noticed also a patchy, red eruption of the skin on the right leg. The next day these eruptions had been also on the other leg and on the arms. About this time the hands, feet, and legs had become swollen and the swelling had been associated with marked pain in all the joints. This condition had subsided after a period of twenty-one days and had recurred at intervals of ninety days. With these attacks there also had been accompanying hematemesis, hematuria, and sometimes blood in the stools. Four years before he came to the clinic his condition had been diagnosed as purpura hemorrhagica. Splenectomy had been performed, and as a result the patient had been better. However, nine months after the operation he had recurrence of symptoms. Since splenectomy, these periods of purpuric manifestation had come on erratically; the time interval had varied from two to nine months. The patient stated that "colds" or "grippe" precipitated an attack.

General examination revealed a well-developed man, and a hemorrhagic eruption, as has been described, in the process of decline. Erythrocytes numbered 4,060,000, leukocytes 6,400, and platelets from 157,000 to 383,000 in each cubic millimeter of blood. Hemoglobin was estimated at 15.8 gm. for each 100 c.c., or 92 per cent. The coagulation time was three and a half minutes, the bleeding time one and a half minutes. There was no retraction of the blood clot at the end of six hours, but complete retraction in seven and a quarter hours.

The prothrombin time was as follows: 2 drops, ten minutes; 3 drops, ten minutes; 4 drops, ten minutes; 5 drops, eleven minutes; 6 drops, twelve minutes; 7 drops, fourteen minutes; 8 drops, fourteen minutes. Because of the history of sudden onset of urticaria and of lesions resembling erythema multiforme coming with the onset of the purpura, the previous diagnosis of purpura hemorrhagica was questioned and the possibility of

purpura of infectious origin was considered. This idea was strengthened by the statement that colds or respiratory infections precipitated an attack.

The tonsils had been cleanly removed and there were no demonstrable tonsillar tags. The teeth were all vital; there was no demonstrable pyorrhea, and there were no teeth with massive fillings. The lymphoid tissue at the base of the tongue was grossly unchanged. In order to eliminate all sources of infection, cultures were obtained from the nasopharynx and were injected intravenously into two rabbits. The rabbits were perfectly well at all times, and necropsy forty-eight hours later failed to reveal any positive or even suggestive evidence of hemorrhages, petechial or otherwise. In order to exclude all possibilities, a culture was made of the patient's prostatic secretion. The first culture remained sterile. The second culture, obtained after thorough massage of the prostate gland, consisted of *Streptococcus viridans* mixed with a few colonies of *Staphylococcus albus*. The freshly isolated cultures in glucose-brain broth were injected intravenously into two rabbits; each received two daily injections of 5 c.c. The first rabbit was chloroformed forty-eight hours after the last injection and necropsy revealed scattered small hemorrhages of the superficial fascia of the outside of the right leg and thigh. Cultures of the blood were sterile. The second rabbit also was chloroformed forty-eight hours after the second injection. The hind thighs and legs, as well as the muscles of the abdomen and those in the region of the axillae, contained multiple, small, discrete, but often confluent, hemorrhages, 0.5 to 5 mm. in diameter, just beneath the superficial fascia. At many such places the inner surface of the overlying pelt also contained a brownish-red discoloration (old hemorrhage). Cultures of the blood contained streptococci and some staphylococci. A mixed culture obtained from the nasopharynx of the patient and a culture of organisms recovered from the blood of one of the rabbits that had been inoculated with the culture from the prostate gland were filed in meat-infusion broth. Three weeks later, subcultures were made and two rabbits were inoculated intravenously with the subculture of material from

the nasopharynx, and two with the subculture of material from the prostate gland. Each rabbit received two injections, on two successive days, of 6 and 7 c.c., respectively. They were chloroformed twenty-four hours after the second injection. Necropsy of the rabbits which received the cultures of material from the nasopharynx revealed no evidence whatsoever of hemorrhages; there were no gross lesions, and all cultures were sterile. In contrast, both rabbits that received injections of the culture

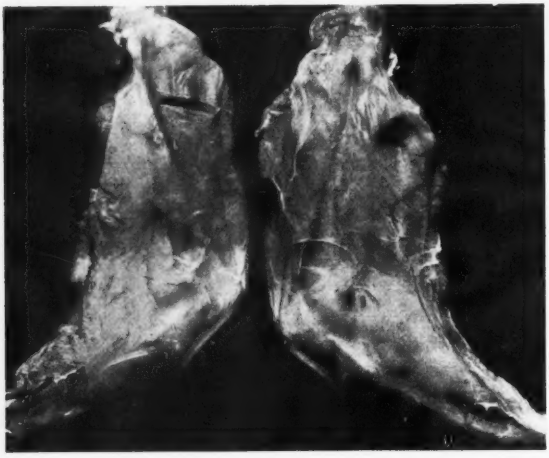

Fig. 178.—Superficial hemorrhagic myositis of the hind extremities of a rabbit, two days after the second of two inoculations that had been given on successive days of 5 c.c. each of a freshly isolated culture of green-producing streptococci and staphylococci. The organisms had been obtained from the prostatic secretion in a case of purpura of infectious origin.

originally obtained from the prostatic secretion had superficial hemorrhagic myositis of the thighs and abdominal muscles, similar to, but not quite as extensive as, the lesions described in the first set of rabbits that received the primary culture of the prostatic secretion. Cultures of the blood and spleen contained green-producing streptococci.

Figure 178 shows the hemorrhages of the thighs. Sections through such hemorrhagic places revealed erythrocytes free in

the tissue, just beneath the fascia or the top layer of muscle in most instances. In these regions streptococci could be found rather sparsely.

COMMENT

Various authors have given diverse reasons for the cause of the purpuric spots. Glanzmann stated that the eruption in essential forms of purpura resembles the rash in serum sickness and he called such forms of purpura, anaphylactoid purpura. He stated the belief that substances, products of proteolysis, having got into the blood, cause the production of poisons which maim the vasomotor fibers, especially of the splanchnic region, and cause a marked fall in blood pressure. These substances act like poisons on the contractile element of the walls of the capillaries. This causes stasis of the blood in the venules and the result is rhexis. French described the phenomenon as hemorrhagic capillary toxicosis. Likewise, in hemorrhages of the bowel the poison attacks the smooth muscle. That the superficial capillaries are injured is verified by Mackay, who stated that there is absence of elastic and muscle fibers in the superficial blood vessels of the affected region.

Because of the rapidity of onset of the lesions and because of the type of lesion resembling erythema multiforme in the case reported here, these symptoms might more accurately be described, according to Hammer, as erythema hemorrhagica or purpura, or as urticaria hemorrhagica. Purpura of infectious origin is not newly discovered. Whether the infection present in the prostate gland could account for all of the symptoms in this case is questionable, for a small nidus could have been present also in the throat and could have been easily overlooked. We deemed the case sufficiently interesting for presentation so that others who might encounter similar cases would not overlook the prostate gland as a possible focus of infection and thereby be in the group discussed by Pelouze, who said: "We no longer sacrifice teeth as we once did, nor do we overlook infected tonsils because they may be 'buried.' We study sinuses, gallbladders, and gastro-intestinal tracts, and then, because the patient states he has never had an attack of gonorrhea, we commonly acquit

the prostate gland without study. And because of this acquittal our patient often fails to reach complete cure." .

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OBSTRUCTION OF THE INFERIOR VENA CAVA

E. G. WAKEFIELD

WHEN a patient presents himself for examination and is found to have abdominal distention and well-developed collateral circulation over the abdominal wall, a presumptuous diagnosis is usually made of cirrhosis of the liver. Such a diagnosis is generally proved correct by subsequent study, but if there is no evidence of cirrhosis of the liver and an abdominal tumor is present, the possibility of obstruction of the inferior vena cava is the second most probable diagnosis. If there is a definite history of phlebitis and of bilateral edema of the lower extremities with subsequent development of collateral circulation over the abdomen and lower part of the thorax, a diagnosis of obstruction to the inferior vena cava is practically certain. Such were the conditions presented in the following case.

A man, aged fifty years, was admitted to The Mayo Clinic April 15, 1929. For ten years he had had remission and relapses of indigestion, which were relieved by taking sodium bicarbonate or by belching. Three months before examination his trouble grew more severe, the abdomen became much distended, and following meals there was considerable borborygmus. There was little pain. Soda did not afford relief, but magnesium sulphate afforded prompt relief. Two weeks before examination he had had a severe sharp pain in the left epigastric region, which passed away after a purgative. His appetite had been good and he had not lost weight. Two years before he had fractured the right femur, and the leg was in a cast for three weeks. As soon as the cast was removed the leg became swollen and was very painful. The swelling extended down to the right foot and up to the

abdomen to about the level of the umbilicus, and involved the left leg. As it slowly subsided the patient noticed large tortuous veins over the legs and the abdomen and the lower part of the thorax. He had noticed that the blood ran "upward" in the large tortuous veins. When the swelling and pain subsided there had been no further discomfort.

The patient appeared to be well developed and fairly well nourished. The abdomen was markedly distended. Over the legs, groins, abdominal wall, and lower part of the thorax were

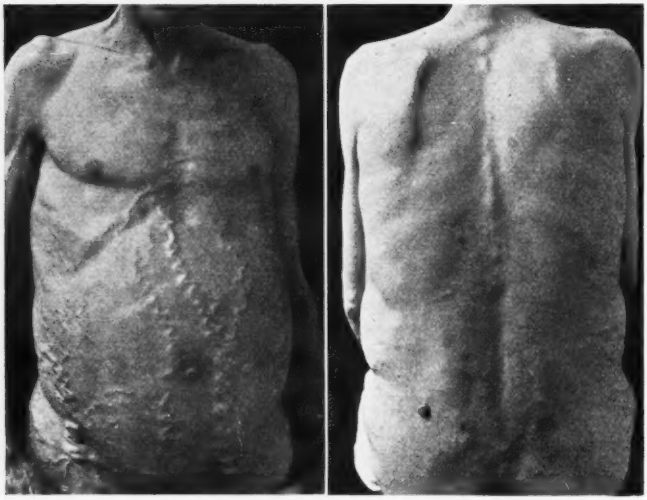

Fig. 179.—Collateral circulation.

large tortuous varicose veins coursing upward. The saphenous veins, the superior and inferior epigastric veins, the lateral thoracic veins, the superficial circumflex iliac veins, the pudendal vein, and many other veins which cannot be definitely assigned to any group, were involved (Fig. 179). When the patient stood, there was marked cyanosis of the legs. The lungs were normal. The heart was displaced upward and the sounds were regular but distant. The systolic blood pressure was 130 and the diastolic 100, measured in millimeters of mercury. Peripheral

sclerosis of the radial vessels was graded 2. Occupying the middle of the epigastrium to below the umbilicus and extending across and filling the left side of the abdomen, was a large, pedunculated tumor which appeared to fluctuate and to transmit percussion impulses. When the patient stood there was considerable bulging in the left flank. The liver and spleen were not palpable. Urinalysis showed a trace of albumin. The Wassermann reaction of the blood was negative. Tests of hepatic function were negative. Serum bilirubin was 3.4 mg. for each 100 c.c., and the van den Bergh reaction was indirect. The blood urea was 48 mg. for each 100 c.c. Roentgenograms of the thorax did not reveal anything unusual. A diagnosis was made of cystic abdominal tumor probably arising from the pancreas, obstruction of the inferior vena cava, and generalized arteriosclerosis with slight hypertension.

At operation, one lipoma weighing 25 pounds and several smaller lipomas, which were attached to the mesentery of the small intestine, were removed. The pathologist reported fibrolipomyxoma with early degeneration.

Convalescence was rapid and uneventful. Seven months after the operation the patient was at work and he felt well except for some frequency of urination. There was no change in the large veins over the legs, abdomen, and thorax.

Since the collateral circulation developed almost two years before the patient had had any definite symptoms, and before abdominal enlargement had been noted by the patient, the tumors can hardly be indicted as the cause of the obstruction of the vena cava.

COMMENT

Thrombosis of the inferior vena cava is rarely autochthonous; usually it extends from the femoral or pelvic veins or is due to abdominal or pelvic infection or tumors. The characteristic symptoms are edema of both lower extremities with the development of collateral circulation. The diagnosis depends on the appearance and the group of veins involved in the collateral circulation. The veins course upward from the groins and flanks over the abdominal wall and lower part of the thorax. They are

large, tortuous, and surprisingly numerous. The group of veins involved are: Superior epigastric veins, the lateral thoracic veins, the superficial circumflex iliac veins, the external pudendal vein, the spinal tributaries of the lumbar veins, the anastomotic trunk of Braune and numerous anastomotic branches without names.

SUMMARY

In the case presented, a fracture of a femur two years before had been followed by phlebitis of the veins of the right leg with edema, which, in turn, was followed immediately by edema of the left leg and abdomen up to the umbilicus. As soon as the edema subsided collateral circulation developed over the abdomen and lower part of the thorax, typical of obstruction of the inferior vena cava. A diagnosis of a cystic tumor of the abdomen, probably cyst of the pancreas, was made. At operation, several lipomas were found. The two conditions were thought to be wholly unassociated.

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